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Letters

Terms for Temperatures

The Appleman-Braham interchange of viewpoints on nomenclature for temperature reductions that go below a predetermined reference point [*Science* **129**, 1296 (1959)] prompts me to observe that none of the terms suggested are as free of ambiguity as they might be, and that some of them can be misleading. The point of contention was the choice between *sub, super,* and *under* as a prefix to the verb *cool* for description of such temperature reductions.

My first point is that the verb itself can be improved. I have found the verb *chill* to be more descriptive in speaking of temperature drops considerably below ambient levels, admittedly not to the same degree that *heating* rather than *warming* distinguishes a substantial rise in temperature, but still enough to establish a suitable distinction in the mind of the reader. English does not provide a common verb that bears quite the same relationship to *cool* that *heat* does to *warm*.

The use of *under* as a prefix for either verb conveys to me an image exactly opposite to the one intended; a system which is "undercooled" means one that experienced a temperature drop *less* than the magnitude to be expected from the context. To a lesser extent, *sub* as a prefix suffers the same handicap.

On the other hand, the prefix *super* implies a marked deviation from the norm, which is not true necessarily for the downward departures from freezing points or saturation temperatures that are meaningful in the systems usually encountered. *Over* describes such a departure better, because it can connote any deviation, no matter how small. It also avoids Braham's objection—a valid one in my opinion—to mixing words of different derivation.

To say that water or a saturated solution is "overchilled" registers in my mind a sharp impression that the system is at temperatures near a critical point (not just "cool"), and that it is to some degree (not necessarily great), below this reference temperature.

H. LEROY THOMPSON
Birmingham, Alabama

European Degrees

I should like to support Seiden's opinion [*Science* **129**, 933 (1959)] that it would be useful from the standpoint of international scientific contacts if some professional group would attempt to standardize the anglicization of continental degrees.

May I suggest that it be considered whether the American Association for the Advancement of Science, representing if possible also the American Medical Association, American Institute of Biological Sciences, American Institute of Chemists, American Chemical Society, and other interested U.S. organizations, could undertake such an endeavor, specifically in collaboration or consultation with the analogous British societies.

D. A. A. MOSSEL
Central Institute for Nutrition and Food Research, Utrecht, Netherlands

Marine Fungi and Limnoria

The recent work by D. L. Ray and D. E. Stuntz [*Science* **129**, 93 (1959)] contains some suggestions and implications concerning our beliefs that need to be corrected.

First, we have not claimed that "marine wood-boring animals do not attack wood or become established in it unless the wood is first invaded and 'conditioned' by marine fungi." However, certain of our studies referred to have indicated that a thorough examination of the role of marine fungi in the destruction of wood certainly is due.

Second, we have not made any statement or implication that "*Limnoria* is unable to attack sterilized wood." There are so many unknown factors in the evidence so far presented that any statement based on this concept would be drawing essentially unsubstantiated conclusions.

Third, we have not expressed a belief that "*Limnoria* will not attack wood until its surface has been 'conditioned'." This "conditioning," if it is of any effect, surely involves physical, chemical, and biological factors, none of which has yet been given adequate study.

A reasonably careful reading of our two articles would show clearly that we were presenting specific observations and results of experimentation concerning marine fungi and were calling attention to the need for careful studies of the interrelationships between the marine organisms which infest submerged wood. We do believe that deterioration is a composite process in which the contribution made by any organism involved in the biologic complex, at any stage in the process, should be given critical evaluation.

ERNEST S. REYNOLDS
SAMUEL P. MEYERS
Marine Laboratory, University of Miami, Miami, Florida

(*Continued on page 46*)

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In Perspective

In January 1958 the National Science Foundation called together 14 abstracting and indexing agencies for a meeting to consider more effective ways of handling scientific information. The meeting was a part of the general reappraisal of our scientific resources in the wake of the first sputnik and more particularly a response to the glowing reports about the success of the Soviet All-Union Institute of Scientific and Technical Information in abstracting and citing the world's scientific and technical literature. Out of it grew the National Federation of Science Abstracting and Indexing Services, a coordinating body made up of both public and private agencies.

But this was only a first step. The National Defense Education Act of 1958, which became law on 2 September 1958, directed the National Science Foundation to establish a Science Information Service which would have the responsibility of providing for more effective dissemination of scientific information. The provisions of the act were reinforced by a presidential directive which strengthened the hand of the foundation in getting cooperation from other federal agencies in carrying out its functions.

For one thing, the U.S. Joint Publications Service is now translating three of the 13 Soviet abstracting journals. These translations are distributed to the appropriate abstracting services through the Office of Technical Services. Thus, American and other scientists who know no Russian have access to a part of the product of the Soviet All-Union Institute of Scientific and Technical Information.

For another thing, there has been a sharp increase in the number of articles abstracted, and there is better coordination among abstracting agencies. G. Miles Conrad, director of *Biological Abstracts*, estimates that in the United States, the number of abstracts and title citations of Soviet publications was 437,000 in 1957 and that it will reach 588,000 in 1959, an increase of 34 percent. In the corresponding years the figure for the Soviet Union rose from an estimated 455,000 to an estimated 480,000 abstracts and citations. (Because of temporary suspension of publications of several issues of the Soviet journals, the latter figure is somewhat uncertain.)

Neither abstracts nor citations are intended to be complete substitutes for the original articles; they serve mainly to lead readers to articles of interest. When these articles are in languages unfamiliar to a large majority of the readers, some provision has to be made for translation. The National Science Foundation has favored a two-pronged approach: translation of the more important Soviet journals in their entirety and selective translation of other journals. Eighteen months ago the number of Soviet journals translated completely was 35 (six of these projects were under NSF support) as compared with 76 today (35 under NSF support); next month another will be added, under a new arrangement: the Optical Society of America will supply to its members both its own journal and the Soviet *Optics and Spectroscopy* in complete translation for the price of a single journal.

In the past, articles selectively translated for government, industry, or universities were often inaccessible. The Office of Technical Services now publishes *Technical Translations*, which lists all available translated articles, and both OTS and the John Crerar Library in Chicago attempt to secure copies of these articles.

Thus, an American scientist now has a much better chance to find out what is going on in his field, both at home and abroad, than he did a year and a half ago. But neither the government nor the abstracting and other services can do the searching for him. He has to take it from there—G.DuS.

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Reasoning Foundations of Medical Diagnosis

Symbolic logic, probability, and value theory aid our understanding of how physicians reason.

Robert S. Ledley and Lee B. Lusted

The purpose of this article is to analyze the complicated reasoning processes inherent in medical diagnosis. The importance of this problem has received recent emphasis by the increasing interest in the use of electronic computers as an aid to medical diagnostic processes (*1*, *2*). Before computers can be used effectively for such purposes, however, we need to know more about how the physician makes a medical diagnosis.

If a physician is asked, "How do you make a medical diagnosis?" his explanation of the process might be as follows. "First, I obtain the case facts from the patient's history, physical examination, and laboratory tests. Second, I evaluate the relative importance of the different signs and symptoms. Some of the data may be of first-order importance and other data of less importance. Third, to make a differential diagnosis I list all the diseases which the specific case can reasonably resemble. Then I exclude one disease after another from the list until it becomes apparent that the case can be fitted into a definite disease category, or that it may be one of several possible diseases, or else that its exact nature cannot be determined." This, obviously, is a greatly simplified explanation of the process of diagnosis, for the physician might also comment that after seeing a patient he often has a "feeling about the case." This "feeling," although hard to explain, may be a summation of his impressions concerning the way the data seem to fit together, the patient's reliability, general appearance, facial expression, and so forth; and the physician might add that such thoughts do influence the considered diagnoses. No one can doubt that complex reasoning processes are involved in making a medical diagnosis. The diagnosis is important because it helps the physician to choose an optimum therapy, a decision which in itself demands another complex reasoning process.

This complex reasoning process must be integrated by the physician with a large store of possible diseases. It is widely believed that errors in differential diagnosis result more frequently from errors of omission than from other sources. For instance, concerning such errors of omission, Clendening and Hashinger (*3*) say: "How to guard against incompleteness I do not know. But I do know that, in my judgment, the most brilliant diagnosticians of my acquaintance are the ones who do remember and consider the most possibilities."

Computers are especially suited to help the physician collect and process clinical information and remind him of diagnoses which he may have overlooked. In many cases computers may be as simple as a set of hand-sorted cards, whereas in other cases the use of a large-scale digital electronic computer may be indicated. There are other ways in which computers may serve the physician, and some of these are suggested in this paper. For example, medical students might find the computer an important aid in learning the methods of differential diagnosis. But to use the computer thus we must understand how the physician makes a medical diagnosis. This, then, brings us to the subject of our investigation: the reasoning foundations of medical diagnosis and treatment.

Medical diagnosis involves processes that can be systematically analyzed, as well as those characterized as "intangible." For instance, the reasoning foundations of medical diagnostic procedures are precisely analyzable and can be separated from certain considered intangible judgments and value decisions. Such a separation has several important advantages. First, systematization of the reasoning processes enables the physician to define more clearly the intangibles involved and therefore enables him to concentrate full attention on the more difficult judgments. Second, since the reasoning processes are susceptible to precise analysis, errors from this source can be eliminated. Of course, the methods presented in this paper are not designed for immediate, direct application; rather, they serve as a suggested basis from which more practical procedures can be developed. However, a consideration of foundations is always essential as the first step in the development of practical applications.

The reasoning foundations of medical diagnosis and treatment can be most precisely investigated and described in terms of certain mathematical techniques. Before material to illustrate these techniques was selected, many of the *New England Journal of Medicine*

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clinicopathological exercises from Massachusetts General Hospital were studied. It has been necessary to simplify the case illustrations in order to demonstrate the calculations in their entirety.

Two well-known mathematical disciplines, symbolic logic and probability, contribute to our understanding of the reasoning foundations of medical diagnosis; a third mathematical discipline, value theory, can aid the choice of an optimum treatment. These three basic concepts are inherent in any medical diagnostic procedure, even when the diagnostician utilizes them subconsciously, or on an "intuitive" level.

As is shown below, the logical concepts inherent in medical diagnosis emphasize the fundamental importance of considering combinations of symptoms or *symptom complexes* in conjunction with combinations of diseases or *disease complexes*. This point is emphasized because often an evaluation is made of a sign or symptom (*4*) by itself with respect to each possible disease by itself, whereas consideration of the combinations of signs and symptoms that the patient does and does not have in relation to possible combinations of diseases is of primary importance in diagnosis.

The probabilistic concepts inherent in medical diagnosis arise because a medical diagnosis can rarely be made with absolute certainty; the end result of the diagnostic process usually gives a "most likely" diagnosis. The logical considerations present *alternative* possible disease complexes that the patient can have; the purpose of the probabilistic considerations is to determine which of these alternative disease complexes is "most likely" for this patient.

The value theory concepts inherent in medical diagnosis and treatment are concerned with the important value decisions that the diagnostician frequently faces when he is choosing between alternative methods of treatment. The problem facing the physician is to choose that treatment which will maximize the chance of curing the patient under the ethical, social, economic, and moral constraints of our society. As is discussed below, Von Neumann's so-called "theory of games" can be used to analyze such value decisions.

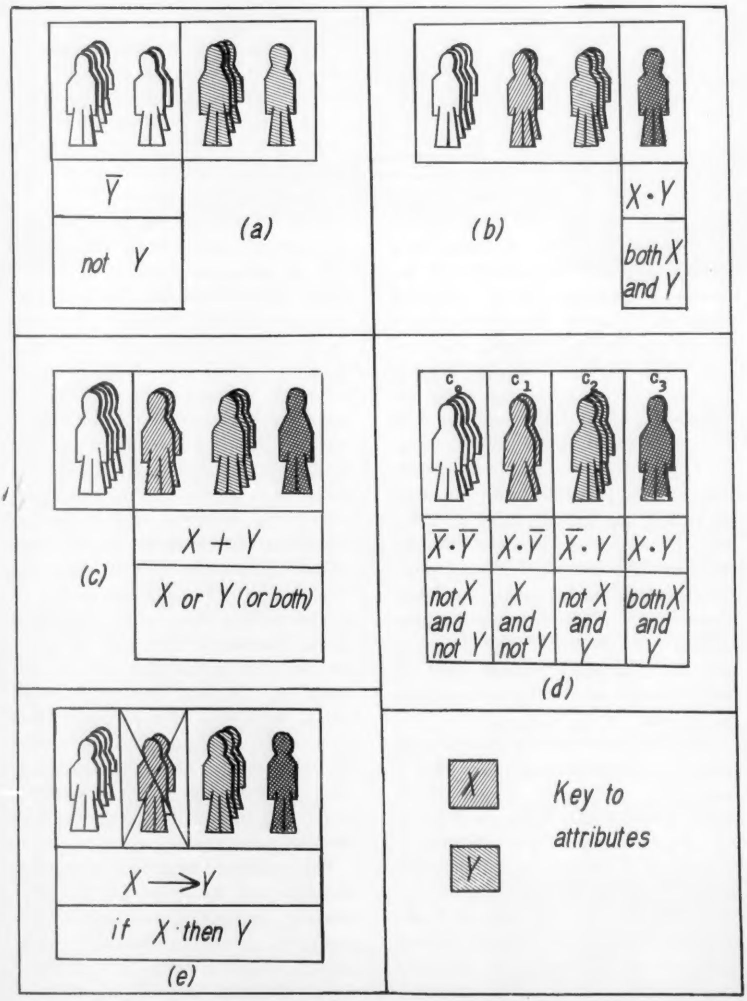

Fig. 1. Combinations of attributes.

Logical Concepts

There are three ingredients to the logical concepts inherent in medical diagnosis; these are (i) medical knowledge, (ii) the signs and symptoms presented by the patient, and (iii) the final medical diagnosis itself. Medical knowledge presents certain information about relationships that exist between the symptoms and the diseases. The patient's symptoms (*4*) present further information associated with this particular patient. With these two sources of available information, and by means of logical reasoning, the diagnosis is made.

Symbolism. The first step in making a logical analysis of this process is to review some symbolism associated with the *propositional calculus of symbolic logic*. Such symbolism enables the more precise communication of the concepts involved in logical processes. The symbols x, y, . . . are used to represent "attributes" a patient may have such as, for instance, a sign "fever" or a disease "pneumonia," and so forth. Corresponding capital letters X, Y, . . . are used to represent statements about these attributes. For example, Y represents the sentence:

The patient has the attribute y.

The negation of this statement:

The patient does not have the attribute y.

is represented by $\overline{Y}$, where the bar (called negation) over the Y indicates "not." The combination of symbols $X \cdot Y$ represents the combined statement:

The patient has both the attribute x and the attribute y.

where the center dot (called logical product) indicates "and." The combi-

Table 1. Symbolic representation of combinations of attributes.

Symbols	Name	Interpretation
$\overline{Y}$	Negation	Not Y
$X \cdot Y$	Logical product	X and Y
$X + Y$	Logical sum	X or Y (or both)
$X \rightarrow Y$	Implies	If X then Y

nation of symbols $X+Y$ represents the combined statements:

The patient has attribute x
or attribute y, or both.

where the plus sign (called logical sum) indicates "or"—that is, the "inclusive or." The sentence:

If the patient has attribute x,
then he has attribute y.

is symbolized by $X \rightarrow Y$.

All these symbols and their meanings are summarized in Table 1. But they can be most easily visualized by considering, for example, the population of patients illustrated in Fig. 1. The cross-hatched patients of Fig. 1*a* have attribute y—that is, they are those for whom Y holds. If we now consider a second attribute x for some of our patients (cross-hatched in the other direction), then Fig. 1*b* indicates these patients for whom $X \cdot Y$ holds. Similarly, Fig. 1*c* indicates those patients for whom $X+Y$ holds. In fact, with two attributes, our patients can be put into four classes, as indicated by C_0, C_1, C_2, and C_3 of Fig. 1*d*.

Figure 1*e* illustrates a population of patients where the attributes x and y have the property that "if X then Y." Here, note that the patients for whom $X \rightarrow Y$ holds are those of C_0, C_2 and C_3 only. The situation C_1 cannot occur (because C_1 represents patients with X but not Y); hence, C_1 has been crossed out.

Of course, in general, more than two attributes are usually considered, and more complicated expressions can be formed by making combinations of attributes. Such expressions are called "Boolean functions" and are generally denoted in terms of the usual functional notation $f(X, Y, \ldots, Z)$. Similarly, for more than two attributes, we can classify the patients into more than four classes C_i. In fact, it is easy to see that for m attributes, there are 2^m possible ways the patients can and cannot have the m attributes—that is, there are 2^m of the classes C_i, namely, $C_0, C_1, \ldots, C_{2m-1}$.

For our purposes, we need only introduce attributes that are symptoms and diseases. Let the symbol $S(1)$ mean, "The patient has symptom 1," and similarly for $S(2)$, and so forth. Let the symbol $D(1)$ mean, "The patient has disease 1," and similarly for $D(2)$, and so forth. In general, a set of n symptoms,

$$S(1), S(2), \ldots, S(n)$$

and a set of m diseases,

$$D(1), D(2), \ldots, D(m)$$

will be under consideration. Which symptoms and diseases are to be included in such sets is usually dictated by the circumstances. For example, an ophthalmologist is interested in a certain collection of symptoms and diseases, whereas an orthopedist is interested in another collection.

Logical problem. By means of our symbolic language, each of the three aforementioned ingredients of medical diagnosis can be expressed in terms of Boolean functions. The relationships between diseases and symptoms that comprise medical knowledge can be expressed as a Boolean function of the diseases and symptoms under consideration, say

$$E(S(1), \ldots, S(n), D(1), \ldots, D(m))$$

Similarly, the symptoms presented by a patient can be expressed as a Boolean function of the symptoms alone, say

$$G(S(1), \ldots, S(n))$$

Then the diagnosis itself can be expressed as a Boolean function of the diseases alone, say

$$f(D(1), \ldots, D(m))$$

To illustrate these three functions E, G, and f, let us for simplicity limit our consideration to two diseases, $D(1)$ and $D(2)$, and two symptoms, $S(1)$ and $S(2)$. Let us first discuss E. Suppose the following statements were made in a diagnostic textbook concerning the relationships between $D(1)$, $D(2)$, $S(1)$, and $S(2)$:

If a patient has disease 2, he must have symptom 1	$D(2) \rightarrow S(1)$
If a patient has disease 1 and not disease 2, then he must have symptom 2	$D(1) \cdot \overline{D(2)} \rightarrow S(2)$
If a patient has disease 2 and not disease 1, then he cannot have symptom 2	$\overline{D(1)} \cdot D(2) \rightarrow \overline{S(2)}$
If a patient has either or both of the symptoms, then he must have one or both of the diseases	$S(1) + S(2) \rightarrow D(1) + D(2)$

Since all of these relations are to hold according to medical knowledge, we have for E:

$$E = [D(2) \rightarrow S(1)] \cdot [D(1) \cdot \overline{D(2)} \rightarrow S(2)] \cdot [\overline{D(1)} \cdot D(2) \rightarrow \overline{S(2)}] \cdot [S(1) + S(2) \rightarrow D(1) + D(2)] \quad (1)$$

To illustrate the G function is much simpler. A particular patient might present symptom 2 and not symptom 1; then we have

$$G = \overline{S(1)} \cdot S(2)$$

Note that symptoms the patient does *not* have are included as well as those the patient does have. If it is not known whether the patient does or does not have a symptom—for example, if the symptom is determined as the result of a laboratory test not yet accomplished, then this symptom does *not* appear explicitly in the function G. Thus, if the patient has symptom 2 and it is not known whether or not he has symptom 1, then $G = S(2)$.

Function f may be illustrated as follows. If the patient has disease 1 and not disease 2, then

$$f = D(1) \cdot \overline{D(2)}$$

Of course, function f is computed when the functions E and G are known. For example, as we shall presently show, if E as illustrated above describes the medical knowledge concerning $D(1)$, $D(2)$, $S(1)$, and $S(2)$, and if a patient presents

$$G = \overline{S(1)} \cdot S(2)$$

then it turns out that

$$f = D(1) \cdot \overline{D(2)}$$

Although we shall discuss a specific example below, it is important to first state the logical problem of medical diagnosis in more abstract terms. The logical aspect of the medical diagnosis problem is to determine the diseases f such that *if medical knowledge* E *is known, then: if the patient presents symptoms* G, *he has diseases* f. In terms of our symbolic language, the problem is to determine a Boolean function f that satisfies the following formula:

$$E \rightarrow (G \rightarrow f) \quad (2)$$

This is the fundamental formula of medical diagnosis. That this is truly the diagnosis in an intuitive sense can be readily seen. For it is easy to show that the fundamental formula can be equivalently written as

$$E \rightarrow (\overline{f} \rightarrow \overline{G})$$

	C_0	C_1	C_2	C_3
$D(1)$	0	1	0	1
$D(2)$	0	0	1	1

Fig. 2. Logical basis for $D(1)$ and $D(2)$.

	C^0	C^1	C^2	C^3
$S(1)$	0	1	0	1
$S(2)$	0	0	1	1

Fig. 3. Logical basis for $S(1)$ and $S(2)$.

which means in a sense that if the diseases f are cured, then the patient's symptoms will disappear. It can be shown that a solution f always exists. We shall actually illustrate below an elementary computational technique for determining the function f in a simple situation involving two symptoms and two diseases; however, for more complicated situations where many more symptoms and diseases are involved, more advanced and powerful techniques for computing f must be used (*5–7*).

Logical basis. To illustrate the application of the elementary computational method to a specific example, we must first consider the concept of a logical basis. Actually, we have already introduced this concept in a preliminary way in Fig. 1*d*, for a logical basis displays all conceivable combinations of the attributes under consideration that a patient may have. For two attributes (as considered in Fig. 1*d*) there are four such combinations. Figure 2 illustrates how these are displayed in a logical basis corresponding to the attributes $D(1)$ and $D(2)$. The 0 indicates that the corresponding disease does not occur; the 1 indicates that it does. Each column C_i represents a *disease complex,* that is, C_0 represents $\overline{D(1)} \cdot \overline{D(2)})$, C_1 represents $D(1) \cdot \overline{D(2)}$, and so forth. The columns represent an *exhaustive* list of conceivable complexes, that is, a patient must fit into one of these complexes. The complexes are *mutually exclusive*—that is, a particular patient can fit into only one of the complexes at a time.

Similarly, we can form a logical basis for two symptoms, as is shown in Fig. 3, where the columns are now labeled by C^k, with a superscript, and represent all conceivable symptom complexes. If we consider the four attributes $S(1)$, $S(2)$, $D(1)$, and $D(2)$, then all conceivable combinations of disease complexes and symptom complexes can be summarized by the columns on the logical basis of Fig. 4. Each column represents a different product $C^k \cdot C_i$; let us denote such a column simply by C_i^k. For example, the demarcated column in Fig. 4 corresponds to $C^1 \cdot C_2$, and we denote it by C_2^1. Thus this column C_2^1 represents the conceivable situation of a patient's having $S(1)$ but not $S(2)$, and at the same time $D(2)$ but not $D(1)$—that is,

$$S(1) \cdot \overline{S(2)} \cdot \overline{D(1)} \cdot D(2)$$

similarly, column C_3^2 (that is, $C^2 \cdot C_3$) represents the case

$$\overline{S(1)} \cdot S(2) \cdot D(1) \cdot D(2)$$

and so forth. For n symptoms and m diseases, the combined logical basis will have 2^{n+m} columns representing all conceivable combinations of symptom-disease complexes. The reader who is familiar with the binary number system will note that the columns of a logical basis with b rows simply form the binary numbers from 0 to $(2^b - 1)$.

Example of elementary computation. Although a logical basis lists all conceivable symptom-disease complex combinations, it is obvious that many of these do not actually occur. Which do occur and which do not occur is information included in medical knowledge, and therefore it is natural for us to look to the E function for such information. Thus the role of the E function that embodies medical science is to reduce the logical basis from all *conceivable* combinations of disease-symptom complexes to only those that are actually *possible.* As an illustration, consider the E function of the above example (see Eq. 1). First note that it contains as a term the expression $D(2) \rightarrow S(1)$. This means that if a patient has $D(2)$ then he must have $S(1)$, and hence the combination of a patient having $D(2)$ and not $S(1)$—that is, $\overline{S(1)}$—cannot occur; thus, for example, column C_2^0, namely

$$\begin{array}{rl} & C_0 \\ S(1) & 0 \leftarrow \\ S(2) & 0 \\ D(1) & 0 \\ D(2) & 1 \leftarrow \\ & C_2 \end{array}$$

cannot occur. Similarly it can be checked that columns C_2^2, C_3^0, and C_3^2 cannot occur, for each of these represents patients who have at least disease $D(2)$ but do not have symptom $S(1)$ (see Fig. 4 and Fig. 1*e*). Also the expression

$$D(1) \cdot \overline{D(2)} \rightarrow S(2)$$

is included in E; hence columns C_1^0 and C_1^1 must be eliminated. From the expression

$$\overline{D(1)} \cdot D(2) \rightarrow \overline{S(2)}$$

we find that columns C_2^2 and C_2^3 must be eliminated. Finally, the expression

$$S(1) + S(2) \rightarrow D(1) + D(2)$$

eliminates columns C_0^1, C_0^2, and C_0^3. Thus the *reduced basis* that includes the medical science information (that is, Fig. 4 with the appropriate columns omitted) is shown in Fig. 5.

We now come to the following point: If the patient presents a particular symptom complex, what possible disease complexes does he have? Consider, for example, a patient that presents the case C^2—that is,

$$G = \overline{S(1)} \cdot S(2)$$

The only column in our reduced basis that contains this symptom complex is C_1^2—that is

$$\begin{array}{rl} S(1) & 0 \\ S(2) & 1 \\ D(1) & 1 \\ D(2) & 0 \end{array}$$

(see Fig. 5). Since this is the only disease-symptom complex combination that can occur (according to medical knowledge) that includes the symptom complex $\overline{S(1)} \cdot S(2)$, it follows that the diagnosis is C_1—that is,

$$f = D(1) \cdot \overline{D(2)}$$

or the patient has disease $D(1)$ but not disease $D(2)$.

As another example, suppose the patient presented C^1—that is,

$$G = S(1) \cdot \overline{S(2)}$$

then we must consider both column C_2^1 and column C_3^1, since both of these columns include the $S(1) \cdot \overline{S(2)}$ symptom complex. Thus there are two possible disease complexes that the patient may have, C_2 or C_3. Thus,

$$f = \overline{D(1)} \cdot D(2) + D(1) \cdot D(2)$$

—that is, the patient has disease $D(2)$ and it is not known whether he has $D(1)$ or not; either further tests must be taken or else medical knowledge cannot tell whether or not he has $D(1)$ under these circumstances.

Next, suppose the patient has $S(2)$,

and it is not known whether he has $S(1)$ or not—that is, C^2 or C^3, or

$$G = S(1) \cdot S(2) + \overline{S(1)} \cdot S(2)$$

In this case we consider $C_1{}^2$, $C_1{}^3$, and $C_3{}^3$, whence the patient has C_1 or C_3—that is,

$$f = D(1) \cdot \overline{D(2)} + D(1) \cdot D(2)$$

or the patient certainly has $D(1)$ but it is not known whether he has $D(2)$ or not.

We have thus demonstrated how, from the reduced basis that embodies medical knowledge and from the symptom complexes presented by the patient, we can determine the possible disease complexes the patient may have, which is the medical diagnosis.

Probabilistic Concepts

Need for probabilities. In the previous section we considered statements such as, "If a patient has disease 2, he must have symptom 2." While such positive statements have a place when, for example, some laboratory tests are being discussed, it is also evident that in many cases, the statement would read, "If a patient has disease 2, then there is only a certain *chance* that he will have symptom 2—that is, say, approximately 75 out of 100 patients will have symptom 2." Since "chance" or "probabilities" enter into "medical knowledge," then chance, or probabilities, enter into the diagnosis itself. At present it may generally be said that specific probabilities are rarely known; medical diagnostic textbooks rarely give numerical values, although they may use words such as "frequently," "very often," and "almost always." However, as is shown below, it is a relatively simple matter to collect such statistics. Since we are considering topics from an essentially academic point of view, we shall assume that the probabilities are known or can be easily obtained, and we shall discuss methods of utilizing such probabilities in the medical diagnosis. Actually, such a discussion makes clear in any particular circumstances precisely which statistics should be taken and presents methods for rapidly collecting them in the most useful form.

Total and conditional probabilities. The first step in discussing a probabilistic analysis of medical diagnosis is to review some definitions and important properties of probabilities. The concept of total probability is concerned with the following question. Suppose we select at random from our population of patients one single patient; what is the chance, or *total* probability, that the patient chosen has certain specified attributes $f(x, y, \ldots, z)$? By definition, the total probability is the ratio of the number of patients that have these attributes to the *total* number of patients from which the random selection is made. If the total number of patients is N, and if $N(f)$ is the number of these patients with attributes f, then the total probability that a patient has attributes f is:

$$P(f) = N(f)/N \tag{3}$$

For example, the probability that a patient has disease complex C_i becomes:

$$P(C_i) = N(C_i)/N \tag{4}$$

The *conditional probability* is analogous to the total probability, where the selection is made only from that subpopulation of patients that have the specified condition. The conditional probability, denoted by $P(G|f)$, that from patients having condition or attributes f, a single patient selected at random will also have attributes G is defined as the ratio of the number of patients with both attributes $G \cdot f$ to the number of patients having attributes f. [Note: In this notation the condition appears to the right, and the attribute of selection to the left, of the vertical bar: $P(\text{attribute}|\text{condition})$.] Thus we can write:

$$P(G|f) = P(G \cdot f)/P(f) \tag{5}$$

For example, the conditional probability that a patient with disease complex C_i has symptom complex C^k becomes:

$$P(C^k|C_i) = N(C^k \cdot C_i)/N(C_i) \tag{6}$$

Probabilistic problem. The results of the logical analysis of medical diagnosis often leave a choice about the possible disease complexes that the patient may

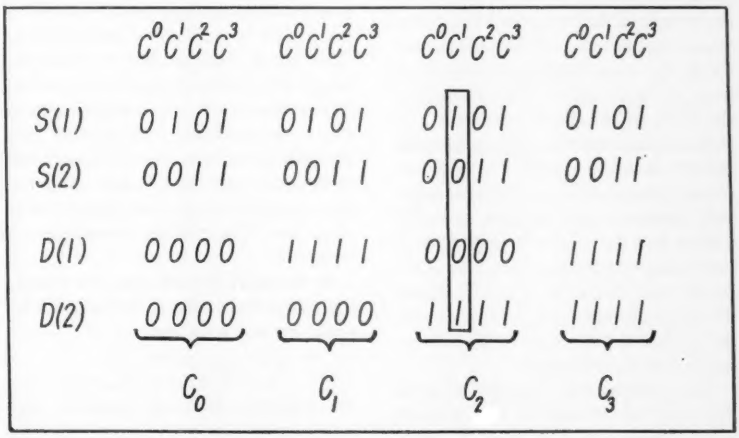

Fig. 4. Logical basis for $S(1)$, $S(2)$, $D(1)$, and $D(2)$.

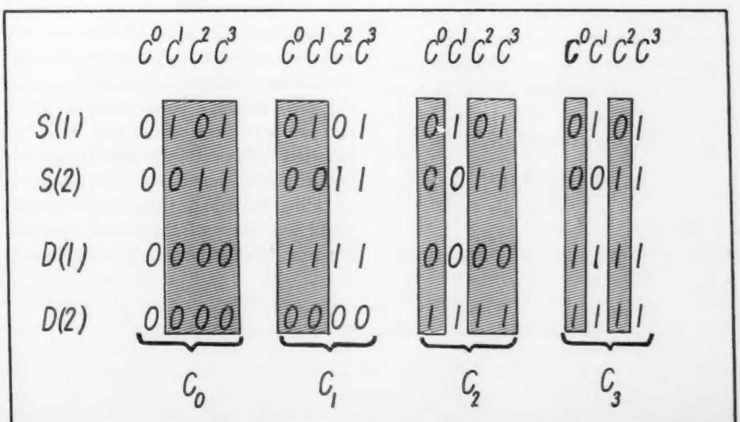

Fig. 5. Reduced basis that includes medical knowledge.

have. The problem now is: Which of these choices is most probable—that is, which of the disease complexes given by the logical diagnosis function f is the patient most likely to have. In terms of conditional probabilities, the probabilistic aspect of the diagnosis problem is to determine the probability that a patient has diseases f where it is known that the particular patient presents symptoms G, that is, the probabilistic aspect of medical diagnosis is to evaluate $P(f|G)$ for a particular patient.

The data upon which the evaluation of $P(f|G)$ is based must, of course, come from medical knowledge. Such medical knowledge is generally also given in the form of conditional probabilities—namely, the probability that a patient having disease complex C_i will have symptom complex C^k, or $P(C^k|C_i)$. The reason medical knowledge takes this form is because this conditional probability is relatively independent of local environmental factors such as geography, season, and others, and depends primarily on the physiological-pathological aspects of the disease complex itself. Thus the study of the disease processes as a cause for the resulting possible symptom complexes can be expressed as such conditional probabilities: of having a symptom complex on condition that the patient has the disease complex. It is interesting to note that this is also the reason most diagnostic textbooks discuss the symptoms associated with a disease, rather than the reverse, the diseases associated with a symptom.

The question that naturally arises at this point is: If medical knowledge is in the form $P(C^k|C_i)$—that is, probability of having the symptoms given the patient having the diseases—then how can we make the diagnosis $P(f|G)$—that is, the probability of having the disease given the patient having the symptoms? The answer lies in the well-known Bayes' formula (*8*) of probability. Let us first discuss the simpler case where $f = C_i$ and $G = C^k$; then it can be shown that

$$P(C_i|C^k) = \frac{P(C_i)P(C^k|C_i)}{\sum\limits_{\omega} P(C_\omega)P(C^k|C_\omega)} \quad (7)$$

where ω under Σ indicates summation

Table 3. Summary of values associated with treatment-disease combinations.

T	C_2	C_3
$T(1)$	90/100	30/100
$T(2)$	10/100	100/100

over all possible disease complexes (that is, if there are m diseases under consideration, then ω takes on values from 0 through $2^m - 1$). The important part of Eq. 7 is the numerator of the right-hand side. It has two factors, $P(C^k|C_i)$ and $P(C_i)$. The former is just the relation between C^k and C_i given by medical knowledge, which we would certainly expect as a factor in the diagnosis. However, observe the latter factor: it is the *total* probability that the patient has the disease complex in question, irrespective of any symptoms. This is the factor that takes account of the local aspects—geographical location, seasonal influence, occurrence of epidemics, and so forth. This factor explains why a physician might tell a patient over the telephone: "Your symptoms of headache, mild fever, and so forth, indicate that you probably have Asian flu—it's around our community now, you know." And the physician is more than likely right; he is using the $P(C_i)$ factor in making the diagnosis.

In the more general case, the following adaptation of Bayes' formula can be made for our purposes:

$$P(f|G) = \frac{\sum\limits^{k\epsilon G}\sum\limits_{i\epsilon f} P(C_i)P(C^k|C_i)}{\sum\limits^{k\epsilon G}\sum\limits_{\omega} P(C_\omega)P(C^k|C_\omega)} \quad (8)$$

Example of a simple computation. Table 2 gives hypothetical probabilities for our example that are consistent with our previous example of two diseases and two symptoms. These conditional probabilities and total probabilities were supposed to have been obtained from clinical statistical data and medical knowledge. We can immediately observe that the conditional probabilities corresponding to columns that were eliminated by means of the logical analysis are zero. This is because these columns represent unrelated disease-symptom combinations, according to medical knowledge, and hence there are no patients having these disease-symptom complexes (see cross-hatched columns of Fig. 5).

Now suppose a patient presented symptom complex

$$G = S(1) \cdot \overline{S(2)} = C^1$$

Logical analysis shows that the diagnosis is

$$f = \overline{D(1)} \cdot D(2) + D(1) \cdot D(2)$$

The problem now is: Which disease complex does the patient most likely have,

$$C_2 = \overline{D(1)} \cdot D(2) \text{ or } C_3 = D(1) \cdot D(2)$$

To solve this problem, we calculate both $P(C_2 \mid C^1)$ and $P(C_3 \mid C^1)$ by means of Eq. 7 and Table 2, as follows:

$$\begin{aligned} P(C_2|C^1) &= [P(C_2)P(C^1|C_2)] \div [P(C_0)P(C^1|C_0) + P(C_1)P(C^1|C_1) + P(C_2)P(C^1|C_2) + P(C_3) + (C^1|C_3)] \\ &= [(25/1000)(1)] \div [(910/1000)(0)] + (50/1000)(0) + (25/1000)(1) + (15/1000)(2/3) \\ &= 25/(25+10) = 5/7 \end{aligned}$$

Similarly, we have

$$\begin{aligned} P(C_3|C^1) &= [(15/1000)(2/3)] \div [(910/1000)(0) + (50/1000)(0) + (25/1000)(1) + (15/1000)(2/3)] \\ &= 10/(25+10) = 2/7 \end{aligned}$$

Hence the chances are 5:2 that the patient has disease 2 but not disease 1, rather than both disease 1 and disease 2.

Next, suppose the patient presented

$$G = S(1) \cdot S(2) = C^3$$

The logical analysis tells us that

$$f = D(1) \cdot \overline{D(2)} + D(1) \quad D(2)$$

That is, the patient has either

$$C_1 = D(1) \cdot \overline{D(2)} \text{ or } C_3 = D(1) \cdot D(2)$$

Determining the conditional probabilities $P(C_1|C^3)$ and $P(C_3|C^3)$ according to Table 2, we find:

$$P(C_1|C^3) = 20/(20+5) = 4/5$$

and

$$P(C_3|C^3) = 5/(20+5) = 1/5$$

Hence the chances are 4:1 that the pa-

Table 2. Illustrative values of $P(C^k|C_i)$ and $P(C_i)$.

$P(C^0\|C_0) = 1$	$P(C^1\|C_0) = 0$	$P(C^2\|C_0) = 0$	$P(C^3\|C_0) = 0$	$P(C_0) = 910/1000$
$P(C^0\|C_1) = 0$	$P(C^1\|C_1) = 0$	$P(C^2\|C_1) = 3/5$	$P(C^3\|C_1) = 2/5$	$P(C_1) = 50/1000$
$P(C^0\|C_2) = 0$	$P(C^1\|C_2) = 1$	$P(C^2\|C_2) = 0$	$P(C^3\|C_2) = 0$	$P(C_2) = 25/1000$
$P(C^0\|C_3) = 0$	$P(C^1\|C_3) = 2/3$	$P(C^2\|C_3) = 0$	$P(C^3\|C_3) = 1/3$	$P(C_3) = 15/1000$

tient most likely has disease 1 and not disease 2 rather than both diseases 1 and 2.

Statistics. In our use of probabilities we have tacitly made one subtle assumption that does not belong in the realm of the reasoning foundations of medical diagnosis, but rather in statistics. The assumption is that even though our probabilities, $P(C_i)$ and $P(C^k|C_i)$, by definition, apply only to a *randomly selected* patient from a *known* population, we of course are applying the same probabilities to a *new* patient (not among the known population) who comes to the physician for diagnosis and treatment. The reason we can apply these probabilities to this patient anyway is beyond the scope of this article; it depends on statistical considerations—considerations which, by the way, have proved exceedingly useful for solving practical problems in many walks of life. However, certain general aspects of the statistical problem can serve to illustrate some properties of our probabilistic approach to medical diagnosis.

Note that the physician has no direct control over which particular person will come to him as a patient at any time, and hence his patients are certainly randomly chosen in this sense. Also note that although the patient is not a member of the known population upon which the probabilities were based, the probabilities will apply to him if he is a person who lives under approximately the same circumstances as those of the known population. By "circumstances" we mean geographical area, local community, season of the year, and so forth.

The important results of these observations are twofold. First, since the probabilities, particularly $P(C_i)$, depend upon such circumstances, then for each physician or clinic there is a $P(C_i)$. That is to say, in general, nearly all the patients of an individual physician or clinic will be subject to the same circumstances. Thus each such physician or clinic will have its own $P(C_i)$ which, in general, will be different at different times. As discussed above, the $P(C_i \mid C^k)$ can be used by many physicians over a longer period of time.

Second, if these probabilities are so variable, from place to place and from time to time, the question arises as to how they can be evaluated at all. The answer to this is based on the fact that once a diagnosis has been made for a patient by a particular physician or clinic at a certain time, the symptom-disease complex combination that this patient has becomes itself a statistic and can be included in a recalculation of the probabilities for this physician or clinic at that time. In other words, the patient for whom the diagnosis has been made automatically becomes a part of the known population upon which the probabilities for those circumstances are based. Thus the known population becomes simply the already-diagnosed cases. Hence the probabilities $P(C_i)$ and $P(C^k|C_i)$ are continuously changing as successive diagnoses are made. Of course, the probabilities should be based on relatively current statistics; hence, after a time, the older cases are dropped from this known population. Actually this recalculation of probabilities is not hard to do. This problem is discussed below.

Value Theory Concepts

Value decisions for treatment: complicated conflict situation. After the diagnosis has been established, the physician must further decide upon the treatment. Often this is a relatively simple, straightforward application of the currently accepted available therapeutic measures relating to the particular diagnosis. On the other hand, and perhaps just as often, the choice of treatment involves an evaluation and estimation of a complicated conflict situation that not only depends on the established diagnosis but also on therapeutic, moral, ethical, social, and economic considerations concerning the individual patient, his family, and the society in which he lives. Similar complicated decision problems frequently arise in military, economic, and political situations; and to aid a more analytical and quantitative approach to these problems, mathematicians have developed "value theory." The striking similarity between these decision problems and the value decisions frequently facing the physician indicate that value theory methods can be applied to the medical decision problem as well. Of the several mathematical forms value theory has taken, we have chosen to discuss that developed principally by Von Neumann (*9, 10*), often called "game theory."

Expected value. One of the basic concepts upon which value theory rests is that of *expected value* (*8*). Suppose we consider 7000 patients, for all of whom two tentative diagnoses, C_2 or C_3, have been made, with probability 5/7 and 2/7, respectively. Suppose, also, that there exists a treatment $T(1)$ that is 90 percent effective against disease complex C_2 and 30 percent effective against disease complex C_3. If we use this treatment, what proportion of the 7000 patients should we expect to cure? The answer is given in terms of the "expected value" of the proportion E, which is the sum of the products of the value of the treatment for curing the disease complex and the probability that a patient has the disease complex. For example, about (5/7) (7000), or 5000, will have disease complex C_2, and of these we expect that 90 percent, or 4500, will be cured by $T(1)$; similarly, for those with disease complex C_3, we expect that 30 percent, or 600, will be cured by $T(1)$. Altogether, we expect that

$$\left[\left(\frac{90}{100}\right)\left(\frac{5}{7}\right)+\left(\frac{30}{100}\right)\left(\frac{2}{7}\right)\right] 7000$$

will be cured by $T(1)$. Here

$$E=\left(\frac{90}{100}\right)\left(\frac{5}{7}\right)+\left(\frac{30}{100}\right)\left(\frac{2}{7}\right)=\frac{51}{70}$$

is the expected value of the proportion of patients cured by $T(1)$.

Suppose, on the other hand, that there is an alternative treatment $T(2)$ for these diseases; it is 10 percent effective against C_2 but 100 percent effective against C_3. The problem is: With which treatment will we expect to cure more patients (see Table 3)? The expected value of the proportion cured by $T(2)$ becomes:

$$\left(\frac{10}{100}\right)\left(\frac{5}{7}\right)+\left(\frac{100}{100}\right)\left(\frac{2}{7}\right)=\frac{25}{70}$$

and hence we would expect to cure more patients with $T(1)$ than with $T(2)$. On the other hand, suppose the probability that a patient has C_2 is 2/7, that he has C_3, 5/7. Then, calculating the expected value of the proportion who will be cured by both $T(1)$ and $T(2)$ respectively, we find:

$$\left(\frac{90}{100}\right)\left(\frac{2}{7}\right)+\left(\frac{30}{100}\right)\left(\frac{5}{7}\right)=\frac{33}{70}$$
$$\left(\frac{10}{100}\right)\left(\frac{2}{7}\right)+\left(\frac{100}{100}\right)\left(\frac{5}{7}\right)=\frac{52}{70}$$

Thus $T(2)$ becomes the treatment of choice.

The process of choosing the best treatment can be described in the terminology of games. There are two players, the physician and nature. The physician is trying to determine the best strategy from his limited knowledge of nature. The matrix representation of values given in Table 3 constitutes the payoffs —what the physician will "win," and nature "lose."

For the values of the treatments as given in Table 3, let us see how the expected value E, and hence the choice of treatment, depends on the probability that the patient has C_2 or C_3. If P is the probability that a patient has C_2, then $(1-P)$ must be the probability that the patient has C_3 (since by supposition the patient has either C_2 or C_3 but not both). Hence, by Table 3, the expected value E_1 with treatment $T(1)$ becomes:

$$E_1 = .9P + .3(1-P)$$

and the expected value E_2 with treatment $T(2)$ becomes:

$$E_2 = .1P + (1-P)$$

Figure 6 illustrates the graphs of these two equations, where the points for $P = 5/7$ and $P = 2/7$, discussed above, are indicated. Hence $T(1)$ is the treatment of choice for P to the right of where the lines cross, and $T(2)$ is the treatment of choice for P to the left of where the lines cross.

Up to now we have considered the value of a treatment with respect to a disease complex as being measured directly by its effectiveness in curing the diseases. This, however, may not always be the case. For example, certain kinds of surgery do involve a marked risk; if the surgery is successful, the patient will be cured or benefited; if it is unsuccessful, the patient may die. Hence the value associated with this treatment is more difficult to define. As an illustration, suppose values were chosen between -10 and $+10$, as is shown in Table 4. Then, if the probability that the patient has C_2 is 5/7 and the probability that he has C_3 is 2/7,

$$E_1 = (5)(5/7) + (-10)(2/7) = 5/7$$
$$E_2 = (-5)(5/7) + (8)(2/7) = -4/7$$

so that $T(1)$ is the treatment of choice. If the probabilities were the other way around, that is, if $C_2 = 2/7$ and $C_3 = 5/7$, then we would have $E_1 = -40/7$, $E_2 = 30/7$, and $T(2)$ would be the treatment of choice.

Two points still require further discussion. First, we have considered our problem from the point of view of many patients all of whom have the diagnosis C_2 or C_3, and we have seen how to choose that treatment which will maximize the number of patients cured or maximize some other value for the patients. However, in private practice, the physician is usually concerned with a single individual patient. A little reflection will show that when we are maximizing the expected number of people cured, we are really maximizing the probability that any *individual* patient will be cured. Hence we need not actually have, say, 7000 patients; we can apply our results to a single patient. The same argument holds when more complicated values are involved.

Table 4. Values associated with treatment-disease combinations.

T	C_2	C_3
$T(1)$	+5	−10
$T(2)$	−5	+8

The second point is that the decision involved for assigning the value to a treatment-disease combination was not discussed at all. Then what is the advantage of our new technique? The advantage is that we have enabled the separation of the *strategy problem* from the *decision of values* problem; however, only the strategy problem was solved. The decision of values problem frequently involves intangibles such as moral and ethical standards which must, in the last analysis, be left to the physician's judgment.

Mixed strategy. In our development of the reasoning foundations of medical diagnosis for treatment, we first sketched the logical principles involved in the diagnosis; based on the alternative diagnoses presented by the logic, we calculated probabilities for these alternatives; based on these probabilities, we sketched a technique for choosing between methods of treatment. However at the present time, as we observed above, data are not generally available to enable the probabilities to be computed; and in rare diseases such data will be difficult to obtain. Hence selection of the method of treatment must frequently be made based on the logical diagnostic results alone. We now consider a method for determining the best treatment under such circumstances.

Again consider 7000 patients with identical diagnoses of C_2 or C_3, and suppose the effectiveness of alternative treatments $T(1)$ or $T(2)$ are as given in Table 3. But this time we do *not* know the probabilities that the patients have C_2 or C_3. Our problem is again to choose that treatment which will insure that we cure the largest number of people—that is, *to maximize the minimum possible number of patients that we expect will be cured.* There are actually three ways we can choose the treatment: (i) treat all patients by $T(1)$, (ii) treat all patients by $T(2)$, and (iii) treat some patients by $T(1)$ and others by $T(2)$. The first two ways are called "pure strategies," the third, a "mixed strategy."

Consider the values of Table 3, and suppose we choose the third way of treatment (which really includes the first two anyway). Let Q be the fraction of patients to be treated by $T(1)$, then $(1-Q)$ is the fraction to be treated by $T(2)$. Observe that if all the patients had C_2, we would expect to cure

$$\left[\frac{90}{100}Q + \frac{10}{100}(1-Q)\right] 7000$$

patients. We have called the bracketed expression $E(C_2)$ and have graphed it in Fig. 7. Similarly, if all the patients had C_3, we would expect to cure

$$\left[\frac{30}{100}Q + \frac{100}{100}(1-Q)\right] 7000$$

patients; we have also graphed this bracketed expression in Fig. 7. Evidently, for a particular value of Q, the lower (thick) line in Fig. 7 represents the minimum number of patients that we can expect to cure. For $Q = .6$, this minimum number is a maximum, and we would expect to cure 58 percent of the patients (or 4060 patients); hence $(.6)(7000)$ patients should be treated by $T(1)$ and the rest, $(.4)(7000)$, should be treated by $T(2)$.

To arrange for such a treatment is easy: Separate the patients at random into two groups, one containing $(.6)(7000) = 4200$ patients, the other containing $(.4)(7000) = 2800$ patients, the former group to receive $T(1)$, the latter $T(2)$. However, there is another way of arranging for such a treatment, as follows: As each patient comes up for treatment, spin the wheel of chance shown in Fig. 8. If the wheel stops opposite one of the numbers 0, 1, 2, 3, 4, or 5, the patient receives $T(1)$; if it stops opposite 6, 7, 8, or 9, the patient receives $T(2)$. Since there is an equal chance that the wheel will stop opposite any number, then about 0.6 of the patients will receive $T(1)$ and 0.4 will receive $T(2)$. This process is called "choosing a random number from 0 to 9." Actually, one does not need to spin a wheel of chance to get random numbers: books have been published containing nothing but millions of random numbers (*11, 12*).

Why do we bring up random numbers when all we really needed to do was

divide our 7000 patients into two groups? To treat the 7000 patients, the two-group technique is perfectly adequate; but let us consider again the physician who is concerned at the moment with a *single* patient. He cannot very well divide up the patient into two groups. To help this physician out, we interpret Q as the ***probability*** that the patient should receive $T(1)$, and then $(1-Q)$ is the probability that the patient should receive $T(2)$. With this interpretation, the above discussion shows that by choosing Q to be .6, the chance or probability of curing the patient is maximized to .58. Hence the physician chooses a single random integer: if it is 0, 1, 2, 3, 4, or 5, the patient gets $T(1)$; if it is 6, 7, 8, or 9, the patient gets $T(2)$. This is the concept of a *mixed strategy* applied to a single case.

Such a method for choosing the treatment may be very hard to appreciate at first contact, but this is just the method used every day when probabilities are applied to single situations. Of course, in actual practice, some further information bearing on the choice of treatment would be sought—that is to say, the formulation of the problem of which treatment to give the patient is far more complicated than that posed by the single problem discussed above. In conclusion, we may quote J. D. Williams (*13*) on the role of game theory:

"While there are specific applications today, despite the current limitations of the theory, perhaps its greatest contribution so far has been an intangible one: the general orientation given to people who are faced with overcomplex problems. Even though these problems are not strictly solvable—it helps to have a framework in which to work on them. The concepts of a strategy, the representations of the payoffs, the concepts of pure and mixed strategies, and so on, give valuable orientation to persons who must think about complicated situations."

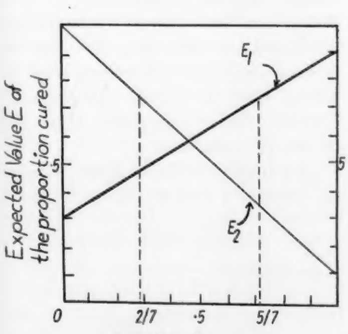

Fig. 6. Mathematical expectation of treatment.

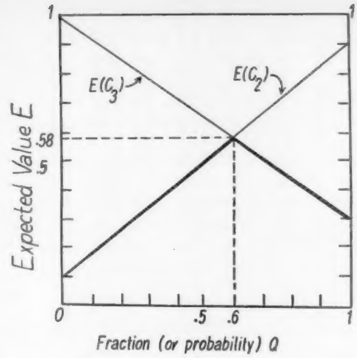

Fig. 7. Mathematical expectation in mixed strategy.

Simplified Illustration

A case history. A 5-week-old female infant was observed by the mother to have progressive difficulty in breathing during a 5-day period. No respiratory problem had been present immediately after birth.

Physical examination showed a well-nourished infant with hemangiomas (blood vessel tumors) on the lower neck anteriorly, on the left ear, and lower lip. The physical examination was otherwise negative, and all the laboratory tests were normal. X-ray examination of the chest showed a mass in the anterior superior mediastinum which displaced the trachea to the right and posteriorly. There was some narrowing of the trachea caused by the mass. Several small flecks of calcium were placed anteriorly within this mass.

The physician is thus faced with this problem: A 5-week-old infant presents increasing respiratory distress which must be relieved or the infant will die. First, what differential diagnosis should he make and, second, what should the treatment be? The physician decided that one or more of three abnormalities might be causing the respiratory distress: (i) a prominent thymus gland [hereafter referred to as $D(1)$], since it is well recognized that a large thymus can cause such distress; (ii) A deep hemangioma in mediastinum, $D(2)$, must be considered because the infant has three surface hemangiomas and therefore should have another hemangioma below the surface of the skin. (The hemangiomas had enlarged since birth.) Also, calcium such as that seen in the mass on the chest x-ray is found in blood vessel tumors; (iii) A dermoid cyst, $D(3)$, could be present in the mediastinum. The calcium in the mass suggests this possibility.

What treatments should be used? The physician decides that some treatment is absolutely necessary and that there are two possibilities, x-ray therapy to the mass or surgery.

There are some arguments for and some against each treatment. This type of problem is susceptible to value theory analysis. The physicians set up the arguments pro and con for each treatment as follows:

1) X-ray therapy to the mass [hereafter referred to as $T(1)$]. *Argument pro.* (i) If the mass is thymus, the x-ray treatment will cause it to decrease in size. (ii) If the mass is a hemangioma composed of small blood vessels, it may decrease with radiation. (iii) This treatment can be done quickly with little discomfort or immediate danger to the patient.

Argument con. (i) Radiation to the mass may cause cancer of the thyroid to develop later (*14*). (ii) Radiation will not affect the mass if it is a dermoid cyst or a large vessel-type hemangioma.

2) Surgery [hereafter referred to as $T(2)$]. *Argument pro.* (i) surgical exploration will permit the surgeon to inspect the mass and to make a definite diagnosis. (ii) If the mass is found to be a dermoid cyst, it can be removed. If the mass is thymus or hemangiomas, partial or total removal may be possible.

Argument con. (i) The infant is subject to the risks of a surgical procedure (these are concerned with general anes-

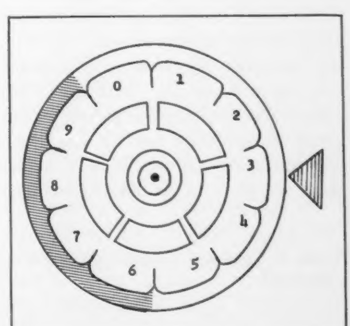

Fig. 8. Gambling wheel.

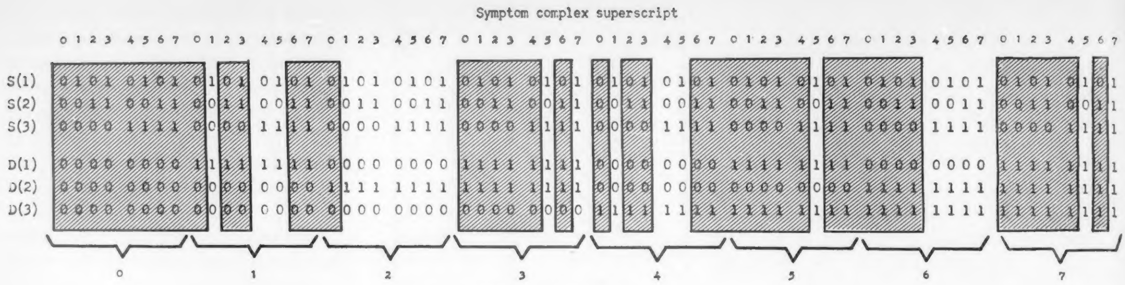

Fig. 9. Reduced logical basis for the illustrative example.

thesia and a chest operation). (ii) If the mass is a hemangioma, an attempt at surgical removal might result in bleeding which would be difficult to control and thereby add to the risk of the operation.

Setting up the illustration. The above case history suggests an appropriate simplification that we can make for purposes of illustration. Let us limit our attention to just the three diseases $D(1)$, $D(2)$, and $D(3)$ (large thymus, deep hemangioma, and dermoid cyst, respectively), the three symptoms $S(1)$, $S(2)$, and $S(3)$ (respiratory distress, several surface hemangiomas, and mediastinal mass on chest x-ray, respectively), and the two treatments $T(1)$ and $T(2)$ (x-ray therapy and surgery, respectively). Of course a realistic application of the techniques developed above would require consideration of the hundreds of diseases and symptoms associated with, say, a particular specialty. However, within the limited space allowed the present article, we are forced to confine our attention to the three diseases and three symptoms suggested by the case history. The discussion of a method permitting the feasible application of our techniques to more realistic circumstances is given in the following section.

We shall now digress for a moment from the case history in order to set up the illustration. Since we are considering only three symptoms, there are $2^3 = 8$ conceivable symptom complexes; for our three diseases there are likewise $2^3 = 8$ conceivable disease complexes; therefore there are $2^{3+3} = 64$ columns in our logical basis that represents all conceivable symptom-disease complex combinations (see Fig. 9). Further, let us suppose that the population of patients under consideration is such that they can have no other symptoms or diseases than those given above, and that each patient must have at least one of the symptoms and at least one of the diseases. Let us suppose that medical knowledge consists of the following three observations:

1. A patient having $D(1)$ and also either $D(2)$ or $D(3)$ must have both symptoms $S(1)$ and $S(3)$ — $D(1) \cdot [D(2) + D(3)] \rightarrow S(1) \cdot S(3)$
2. If a patient does not have $D(2)$ then he does not have $S(2)$ — $\overline{D(2)} \rightarrow \overline{S(2)}$
3. If a patient does not have $D(1)$ but does have both $D(2)$ and $D(3)$, then he has symptom $S(3)$ — $\overline{D(1)} \cdot D(2) \cdot D(3) \rightarrow S(3)$

Under these observations of medical knowledge and under the limitations imposed on the population of patients under consideration, Fig. 9 represents the reduced basis embodying medical knowledge, where the noncrosshatched columns represent possible symptom-disease complex combinations consistent with medical knowledge and the population of patients selected.

Examples of logical diagnosis. Now we are ready to return to our case history. Here the patient presented symptoms $S(1)$, $S(2)$, and $S(3)$—that is,

$$G = S(1) \cdot S(2) \cdot S(3)$$

By the technique described above, it is easy to see the logical diagnosis:

$$f = \overline{D(1)} \cdot D(2) \cdot \overline{D(3)} + D(1) \cdot D(2) \cdot \overline{D(3)} + \overline{D(1)} \cdot D(2) \cdot D(3) + D(1) \cdot D(2) \cdot D(3) = D(2)$$

which means that the patient certainly has $D(2)$, and may or may not have $D(1)$ and $D(3)$. Here, then, the logical diagnosis results in four possible disease complexes that the patient may have.

Consider next a patient that presents symptoms $S(1)$ and $S(2)$, but where the x-ray has not yet been taken—that is, $G = S(1) \cdot S(2)$. By the above techniques, we find that the logical diagnosis

$$f = \overline{D(1)} \cdot D(2) \cdot \overline{D(3)} + D(1) \cdot D(2) \cdot \overline{D(3)} + \overline{D(1)} \cdot D(2) \cdot D(3) + D(1) \cdot D(2) \cdot D(3)$$

Note that this is the same diagnosis as for the patient with symptoms $G = S(1) \cdot S(2) \cdot S(3)$. In other words, if, when the x-ray was taken, positive results were obtained, the diagnosis remains the same as it was before the x-ray results were known. On the other hand, suppose the x-ray turned out negative; then the patient's symptoms would be

$$G = S(1) \cdot S(2) \cdot \overline{S(3)}$$

whence it is easy to see that the diagnosis becomes

$$f = \overline{D(1)} \cdot D(2) \cdot \overline{D(3)}$$

In this case the additional information obtained from the x-ray film enabled the diagnosis to be reduced from four disease complex possibilities to a unique disease complex diagnosis. This example illustrated the interesting fact that additional diagnostic information may not always result in further differentiation between disease complexes, depending on the circumstances.

As a final example of logical diagnosis, consider a patient that presents

$$G = \overline{S(1)} \cdot \overline{S(2)} \cdot S(3)$$

Here we find

$$f = D(1) \cdot \overline{D(2)} \cdot \overline{D(3)} + \overline{D(1)} \cdot D(2) \cdot \overline{D(3)} + \overline{D(1)} \cdot \overline{D(2)} \cdot D(3) + \overline{D(1)} \cdot D(2) \cdot D(3)$$

Thus the patient must have one of these

Table 5. Values of treatments for disease complexes.

T	C_1	C_2	C_4	C_6
X-ray $T(1)$	+3	−2	−3	−2
Surgery $T(2)$	−2	+6	+10	+8

four possible disease complexes. In this case the logical diagnosis, while narrowing down the possibilities, does not seem sufficient. Therefore let us determine which of these disease complexes the patient most probably has.

Examples of probabilistic diagnosis. In order to present these examples we must have a table of conditional and total probabilities. In Fig. 10 we present such a table; however the numbers in the table do not have any basis in fact, they were just made up for the purposes of the illustration. They are, however, self-consistent in themselves and consistent with the logical assumptions made above. The cross-hatched probabilities are all 0 and correspond to symptom-disease complex combinations that are not possible according to medical knowledge.

Consider the patient with symptom complex

$$G=\overline{S(1)}\cdot\overline{S(2)}\cdot S(3)=C^4$$

We found by logical analysis that the patient can have one of the following disease complexes:

$$D(1)\cdot\overline{D(2)}\cdot\overline{D(3)}=C_1$$
$$\overline{D(1)}\cdot D(2)\cdot\overline{D(3)}=C_2$$
$$\overline{D(1)}\cdot\overline{D(2)}\cdot D(3)=C_4$$
$$\overline{D(1)}\cdot D(2)\cdot D(3)=C_6$$

Hence, by the techniques described above, we have:

$$P(C_1|C^4)=[(.600)(.333)]\div[(.600)(.333)+(.150)(.067)+(.050)(.300)+(.005)(.200)]=.885$$

and, similarly,

$$P(C_2|C^4)=.044$$
$$P(C_4|C^4)=.067$$
$$P(C_6|C^4)=.004$$

Thus it becomes clear that the patient most likely has

$$C_1=D(1)\cdot\overline{D(2)}\cdot\overline{D(3)}$$

—that is, an enlarged thymus only.

Analysis of the treatment. Let us continue further with this case and determine the treatment of greatest value for the patient. For this we need a table giving the values of the two treatments under consideration for each of the disease complexes the patient may have. To fill in this table we have used the physician's considered judgment with regard to the pro and con of each treatment in relation to the disease complex. The values have been chosen between +10 and −10, the greatest value (the best treatment for a particular situation) being +10, the smallest (for the worst treatment) being −10 (see Table 5). If statistics were available on the outcomes of the different treatments for the various disease complexes, then the judgment could be replaced by a calculated probabilistic value. However, this cannot always be done in general, for the value of some treatments may involve ethical, social, and moral considerations as well.

Symptom complex superscript

Disease complex subscript	0	1	2	3	4	5	6	7	P(disease complex)
0	0	0	0	0	0	0	0	0	0.000
1	0	.167	0	0	.333	.500	0	0	.600
2	0	.067	.067	.200	.067	.167	.167	.265	.150
3	0	0	0	0	0	.333	0	.667	.150
4	0	.100	0	0	.300	.600	0	0	.050
5	0	0	0	0	0	1.000	0	0	.040
6	0	0	0	0	.200	.200	.200	.400	.005
7	0	0	0	0	0	.200	0	.800	.005

P(symptom complex | disease complex)

Fig. 10. Values of conditional probabilities and total probabilities for the illustrative example.

For our patient who presented symptoms

$$G=\overline{S(1)}\cdot\overline{S(2)}\cdot S(3)$$

we determine for the value of treatment $T(1)$ (the x-ray treatment) by means of the techniques described above, as follows:

$$(3)(.885)-(2)(.044)-(3)(.067)-(2)(.004)=2.358$$

On the other hand, the value of treatment $T(2)$ becomes

$$-(2)(.885)+(6)(.044)+(10)(.067)+(8)(.004)=-.804$$

Obviously, then, the treatment of greatest value to this patient is $T(1)$, the x-ray treatment.

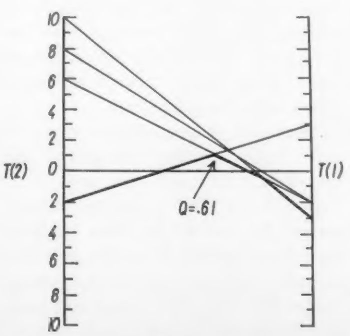

Fig. 11. Determining the best treatment.

On the other hand, suppose we did not know or could not calculate the probabilities $P(C_1|C^4)$, $P(C_2|C^4)$, $P(C_4|C^4)$, and $P(C_6|C^4)$ due to lack of sufficient statistical data or for other reasons. The problem is to choose the treatment which will maximize the minimum gain for the patient. The graphical solution of this problem according to the techniques discussed above is given in Fig. 11. Hence $T(1)$ should be chosen with probability 0.61 over $T(2)$ with probability 0.39.

Conditional Probability or Learning Device

A device often called a conditional probability or learning machine can be used to implement the foregoing logical and probabilistic analysis of medical diagnosis. The particular form of such a device that we shall describe was chosen for its extreme simplicity and ready availability. It can collect data rapidly, and it easily recalculates the probabilities at each use. With such a device the variation of $P(C_i)$ with location, season, and so forth, can be checked as well as relative stability of $P(C^k|C_i)$. As described here, it is essentially an experimental tool, but undoubtedly more sophisticated forms of the device could be further developed.

Consider the logical analysis of medical diagnosis first. In a realistic application perhaps 300 diseases and 400 symptoms must be considered as, for example, might occur within a medical specialty. The logical basis for such a set of symptoms and diseases would require 2^{700} columns (more than 10^{200}) from

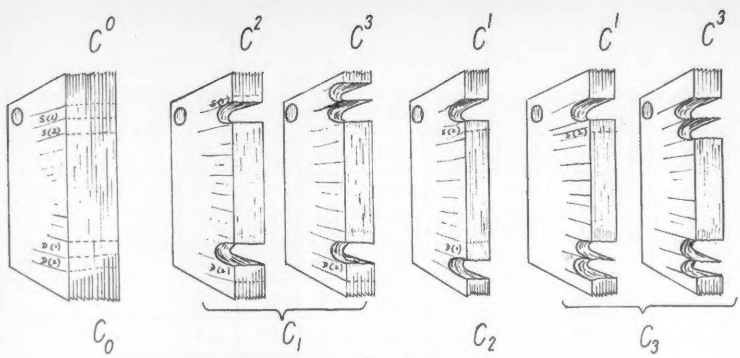

Fig. 12. Cards notched to indicate columns of logical basis.

which the elimination of columns for the reduced basis would be made. This is obviously impracticable. However, the columns to be eliminated correspond to disease-symptom complexes that will never occur; the reduced basis corresponds to columns that will occur. Hence, by listing many cases by disease-symptom complex combination, the reduced basis will soon be generated. This can be done, for example, with marginal notched cards, as follows: Positions along the edge of a card are assigned to the diseases and symptoms under consideration. After a case has been diagnosed, the positions on the edge of a single card are notched corresponding to the diseases the patient has, as well as the presented symptoms. This card then represents a column of the desired reduced basis. In this way the entire reduced basis can soon be generated (see Fig. 12).

The probabilistic analysis of medical diagnosis is obtained by notching a card for every patient who has been diagnosed. Then there will be, in general, more than one card representing a single column of the logical basis. The number of cards representing columns $C^k \cdot C_i$ is then just $N(C^k \cdot C_i)$ of Eq. 6. After a

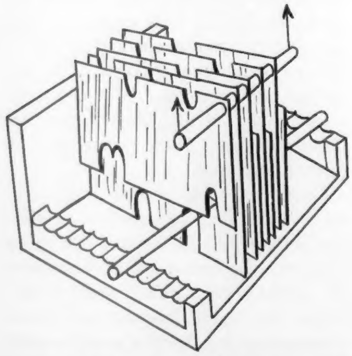

Fig. 13. Sorting the cards.

sufficient number of patients have been so recorded—that is, after a sufficient number of disease-symptom complex combination cards have been obtained—the entire deck of such cards is ready to be used.

The cards are sorted as illustrated in Fig. 13. To separate those cards that are notched in a certain position from those that are unnotched in that position, put a rod in the corresponding position and the notched cards will fall; the unnotched cards will not fall. Then, by means of a rod through the holes in the upper right-hand corner of the cards, the unnotched cards are removed from the notched ones.

To make a diagnosis, sort out those cards that correspond to the symptom complex presented by the patient. The disease complex part of these cards gives all possible disease complexes the patient can have. Separate these cards by the symptom complexes: the thicknesses of the resulting separated decks will be proportional to the probability of the patient's having the respective disease complexes (see Fig. 14).

To determine $P(C_i)$, sort the cards for C_i; then $P(C_i)$ is the ratio of the thickness of the sorted cards to the thickness of the entire deck of cards. To determine $P(C^k|C_i)$, sort the cards for C_i and measure their thickness; then sort these for C^k and measure their thickness; then $P(C^k|C_i)$ is the ratio of the former to the latter measurements.

After each diagnosis is made, a card is notched accordingly and placed with the deck. Old cards are periodically thrown away. This keeps the statistics current. In general, the decks will grow exceedingly rapidly. In a clinic it is often normal to diagnose over 100 patients per day; at this rate only 10 days will result in 1000 cards.

It is important to observe that we are using past diagnoses to aid in making future diagnoses. Any wrong past diagnoses may therefore lead to a perpetuation of errors. Hence it is clear that only carefully evaluated or definitely verified diagnoses should be used in making up the deck, or at least there should be provision for review and removal of incorrect diagnoses.

Conclusions

Three factors are involved in the logical analysis of medical diagnosis: (i) medical knowledge that relates disease complexes to symptom complexes; (ii) the particular symptom complex presented by the patient; (iii) and the disease complexes that are the final diagnosis. The effect of medical knowledge is to eliminate from consideration disease complexes that are not related to the symptom complex presented. The resulting diagnosis computed by means of logic is essentially a list of the possible disease complexes that the patient can have that are consistent with medical knowledge and the patient's symptoms. Equation 2 is the fundamental formula for the logical analysis of medical diagnosis.

The "most likely" diagnosis is determined by calculating the conditional probability that a patient presenting these symptoms has each of the possible disease complexes under consideration. This probability depends upon two contributing factors. The first factor is the conditional probability that a patient

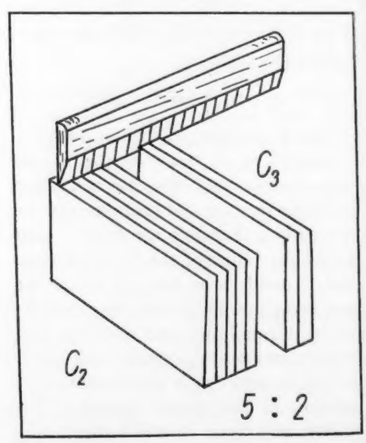

Fig. 14. For a patient presenting symptom complex C^1, the conditional probabilities for diagnoses C_2 and C_3 are read from the respective thicknesses of the decks as $P(C_2|C^1) = 5/(5+2)$ and $P(C_3|C^1) = 2/(5+2)$.

with a certain disease complex will have a particular symptom complex (that is, just the reverse of the afore-mentioned conditional probability); it remains relatively independent of local factors and depends primarily on the physiopathological effects of the disease complex itself. The second factor is the effect on the medical diagnosis of the circumstances surrounding the patient or, more precisely, the total probability that *any* person chosen from the particular population sample under consideration will have the particular disease complex under consideration; this may depend on the geographical location of the population sample, or the season when the sample is chosen, or whether the population sample is chosen during an epidemic, or whether the sample is composed of patients visiting a particular type of specialist or clinic, and so forth.

The afore-mentioned probabilities are continually changing; each diagnosis, as it is made, itself becomes a statistic that changes the value of these probabilities. Such changing probabilities reflect the spread of new epidemics, or new strains of antibiotic-resistant bacteria, or the discovery of new and better techniques of diagnosis and treatment, or new cures and preventive measures, or changes in social and economic standards, and so forth. This observation emphasizes the greater significance and value of current statistics; it depreciates the significance of past statistics. Equation 8 above, which is an adaptation of Bayes' formula, summarizes the probabilistic analysis of medical diagnosis.

Use of value theory enables the systematic computation of the optimum strategy to be used in any situation. It does not, however, determine the values of the treatments involved. It is quite evident that the choice of such values involves intangibles which must be evaluated and judged by the physician. However, by clearly separating the strategy problem from the values judgment problem, the physician is left free to concentrate his whole attention on the latter. One of the most important and novel contributions to the value theory for our purpose is the concept of the mixed strategy for approaching value decisions.

The mathematical techniques that we have discussed and the associated use of computers are intended to be an aid to the physician. This method in no way implies that a computer can take over the physician's duties. Quite the reverse; it implies that the physician's task may become more complicated. The physician may have to learn more; in addition to the knowledge he presently needs, he may also have to know the methods and techniques under consideration in this paper. However, the benefit that we hope may be gained to offset these increased difficulties is the ability to make a more precise diagnosis and a more scientific determination of the treatment plan (*15*).

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Mathematical Inutility and the Advance of Science

Should science entice the mathematician from his ivory tower into Solomon's House?

Carl B. Boyer

A few years ago institutions of learning were cutting requirements in mathematics and foreign language, and Phi Beta Kappa, worried about the survival of the liberal arts, took the drastic step of establishing for initiates minimum requirements in language and mathematics. Today the attitude has changed; but if the contemporary return to favor of mathematics results from a panicky concern for defense, the revival may be short-lived. Thus it is that mathematicians find themselves in the equivocal position of endorsing the demands for increased mathematical training at the same time that they look askance at the motives. Training in mathematics is just as appropriate for philosophers and statesmen as for sputnik-builders; but we shall argue here a more modest thesis concerning the role of mathematics in science, raising a voice in protest against two extreme views. One of these was forcefully expressed in 1941 by G. H. Hardy in *A Mathematician's Apology* (*1*): "It is not possible to justify the life of any genuine professional mathematician on the ground of the 'utility' of his work. . . . I have never done anything 'useful.' No discovery of mine has made, or is likely to make, directly or indirectly, for good or ill, the least difference to the amenity of the world."

The only usefulness he granted mathematics was as an "incomparable anodyne." Hardy went so far as to distinguish between what he called "real" mathematics and "trivial" mathematics —the former being nonuseful, the latter "useful, repulsively ugly and intolerably dull."

Where Hardy rejoiced that the remoteness of mathematics from ordinary human activities keeps it "gentle and clean," Lancelot Hogben, at the other extreme, in 1937 wrote in *Mathematics for the Million* (*2*, p. 36) that "mathematics has advanced when there has been real work for the mathematician to do, and . . . it has stagnated whenever it has become the plaything of a class which is isolated from the common life of mankind." Both of these extreme views do violence to the history of mathematics and science. History indicates on the one hand that the growth of mathematics and the concomitant advance of science are not chiefly the result of utilitarian pressures, but it teaches also that activities of mathematicians which once appeared to be inconsequential have in the end been of far-reaching significance in the growth of science. Paradoxically, the mathematician seems to have been most useful to science when the apparent inutility of his activity was especially marked. Today, especially, surrounded as we are by pressures of immediacy and expediency, it is necessary to look beyond the caricature of the mathematician as a glorified calculator and to appreciate the part that pure mathematics has played in the long-range growth of science.

Pre-Hellenic Mathematics

It was customary, a generation ago, to argue that pre-Hellenic mathematics was entirely practical, but it is obvious now that this picture was overdrawn. Some of the problems in the Ahmes papyrus, for example, are far from utilitarian in nature; and the mathematical inutility in the Egypt of almost four thousand years ago is matched in the Mesopotamian valley of the same period by an instance recently uncovered by Neugebauer. Indefinitely many right triangles with integral sides were known to the Babylonians, for they had the equivalent of a formula for such Pythagorean triads. If p and q are arbitrary integers, with $p > q$, then $p^2 - q^2$, $2pq$, and $p^2 + q^2$ form such a triple of numbers. This result, one of the most remarkable from Old-Babylonian mathematics, is a sophisticated bit of number theory far removed from the hope of immediate utility.

It becomes clearer all the time that mathematical inutility was not unknown in the pre-Hellenic period; but with the Greeks it seems to have become a passion. Greek mathematics started out soberly enough with an eye to the practical. Geometry took its name from the measurement of the earth, and soon it was projected into the heavens; arithmetic promptly found applicability in the Pythagorean discovery that music is "number in motion." But then, probably toward the beginning of the last third of the 5th century B.C., came a discovery which was poles removed from the world of the practical man, and this left a deeper mark on mathematics than has any other single event in its history. Two line segments, it was found, might be such that the ratio of their lengths is not expressible as a ratio of integers. That the diagonal of a square, for example, is incommensurable with its side is of no consequence for the engineer with his slide rule, but in Greece this devastating discovery paved the way for the classical deductive development of mathematics. Ultimately, of course, the deductive method spilled over into the sciences, for it was found to have practical, as well as esthetic, value.

The 5th century B.C. bequeathed also to mathematics the three famous problems of antiquity—the duplication of the cube, the squaring of the circle, and the trisection of the angle—and the better half of later Greek developments centered about these. Inasmuch as craftsmen of the time could solve each of these with a precision that would challenge the keenest senses to find a flaw, the problems made sense only to the impractical geometer, and, as was discov-

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ered in modern times, all three of them are, as presented, impossible of solution. Could anything be more futile than to tackle problems which are meaningless to the practitioner and beyond the power of the scholar? History here has amply vindicated the activities of the ivory-tower mathematician, for the search for solutions led to discoveries without which modern science as we know it would have been unthinkable. Conic sections, for example, seem to have been discovered by Menaechmus, tutor of Alexander the Great, in the course of his efforts to duplicate the cube, and although the utility of the ellipse, parabola, and hyperbola escaped Greek scientists, we know that without the speculations of Menaechmus there might have been no laws of Kepler, no law of gravitation, and no lunik.

Eudoxus and the Great Triumvirate

At the Academy of Plato, as among the Pythagoreans, mathematics was a class-related subject far removed from the common life of mankind, and yet the subject flourished exceedingly. The chief contribution of Eudoxus, the outstanding mathematician associated with Plato, was a theory of proportion which is the equivalent of modern definitions of real number, and it is to be doubted that any practical scientist has had occasion to use the principle of Eudoxus or can tell what a real number is. Eudoxus also had a hand in the method of exhaustion, and this was about as impractical a forerunner of the calculus as could be imagined. Nevertheless, without Plato, the "maker of mathematicians," and the work of Eudoxus, the bulk of what we think of as Greek mathematics would not have developed.

The last century of the Hellenic period might be called the "heroic age," for it was then that the characteristically Greek problems and principles were formulated. During the "golden age" which followed, these were elaborated by the great triumvirate of Euclid, Apollonius, and Archimedes. The earlier sections of Euclid's *Elements*—those included in modern elementary textbooks —have a flavor of practicality, but the deeper one goes, the further the material departs from the ordinary world; one finds a proof of the infinity of primes, a formula for perfect numbers, and the crowning Platonic theorem that there are but five regular solids. In the *Conics* of Apollonius are elaborated the properties of curves, which at the time were beautiful and impractical, for the ellipses which we see in the heavens, the hyperbolas which are formed by our lamp shades, and the parabolas we descry in our suspension bridges were not there for the Greeks. Even the quadratures of Archimedes, which anticipated the now indispensable integral calculus, had at the time little utility; and Archimedes' most sophisticated treatise, *On Spirals,* was largely a mental exercise in circle-squaring and angle-trisecting.

Sharp Decline

Conflicting conjectures have been advanced to account for the sharp decline in mathematics following the great triumvirate, but there is general agreement on one aspect—an admitted transfer of interest from pure to applied mathematics. Under the practicalist theory the shift in interest to the popular fields of astronomy and mensurational geography should have been a catalyst for rapid mathematical development, not the herald of centuries of doldrums. Let this be a warning to those who would equate mathematics and measurement, or who would espouse the fragile thesis of Tobias Dantzig, in *Number, the Language of Science* (1930), quoted (with approval) by Hogben (*2*, p. vii): "It is a remarkable fact that the mathematical inventions which have proved to be the most accessible to the masses are also those which exercised the greatest influence on the development of pure mathematics."

I have mentioned above the mathematical inventions of greatest influence in the pure mathematics of the Greeks, and these inventions were neither accessible nor of interest to the masses. There was in ancient Greece another type of mathematics which had wide appeal. Computation and arithmetic methods, stemming from Babylonian views, were what concerned the vast majority—not axiomatics—and the place of Heron and Diophantus becomes clearer when one regards them as representatives of a tradition which always was present in Greece but which shows through only rarely because of the loss of ancient works. Occasionally both traditions—the higher axiomatic or nonutilitarian stream and the lower arithmetic or utilitarian current—appear in one and the same individual. Ptolemy's *Almagest,* for example, is akin to classical geometry, while his astrological *Tetrabiblos* adopts the Babylonian arithmetical devices, and the verdict of history has been that the theoretical *Almagest* was more influential in the advance of science than the pragmatical *Tetrabiblos.*

No better illustration of the baneful effect of the cold breath of utility upon the ardor of the mathematician can be found than in ancient Rome, where the consequence for science of the Roman contempt for mathematical inutility is too well known to require repetition here. Let us hope that history will not repeat itself in this respect and that a tough-minded concern today for the immediate and obvious needs of national defense—just such as the Romans had in mind—may not stifle the legitimate interests of the pure mathematician. Administrative agencies in this country (and apparently in Russia also) thus far have been very far-seeing in this respect and have generously supported basic research, but if the public clamor for more mathematics in the schools were to result merely in fostering development of expedient techniques, the results could be tragic indeed.

The consequences of a lack of interest in the principles of mathematics, as distinct from a concern with practical outcomes, can be seen in the medieval civilizations—Latin, Greek, Chinese, Hindu, and Arabic. Not one of them had a vigorous tradition of pure mathematics and, interestingly enough, none was strong in science. Much has been made of the so-called Hindu-Arabic system of numeration, but even granted that it was an invention of the Hindus (which is not definitively established), it should be noted that the system involved no principles not known in antiquity, and that with it the Hindus and Arabs were able to do but little. Only later, in 16th-century Europe, was a significant mathematical advance made.

The Renaissance and Mathematics

A facile explanation of the opening of the new age sometimes is found in the rise of a merchant class with practical computational needs, or in the explorations which posed geographical problems, or in the establishment of closer relations between the scholar and the artisan, but the revival in mathematics does not fit neatly into any of these. Apart from the recovery of the Greek

treatises in pure geometry, the event which marked the opening of a new era was the publication of the algebraic solution of the cubic equation. On the surface this looks like an eminently practical result, but nothing could be more deceptive. The formula which Del Ferro and Tartaglia discovered and which Cardan published in 1545, just two years after the epoch-making treatises of Copernicus and Vesalius, was not then, and is not now, of use to the applied mathematician or the practicing scientist. It gave a strong fillip to the pure mathematician's pursuit of algebra, but it did not satisfy the practitioner's need for a practical device for getting approximations to the roots.

Nevertheless, the radical solution of the cubic did in the end stimulate the advance of science—indirectly, and in a rather curious way which well illustrates the unexpected role that mathematical inutility plays. The new formula called attention to imaginary numbers, for in some mysterious way they were bound up with the real roots in the so-called irreducible case. Cardan said of the arithmetic in this case that it is "as subtle as it is useless," and Bombelli, his contemporary, described it as "a wild thought, in the judgment of many; and I too was for a long time of the same opinion." Today any electrical engineer can attest to the ultimate utility of such useless wild thoughts on imaginary numbers; but these numbers at first were rejected by practical men, and even by some not generally regarded as excessively utilitarian. Of them Simon Stevin wrote, "There are enough legitimate things to work on without need to get busy on incertain matter"; and only occasionally were men bold enough to handle these quantities which Leibniz regarded as a sort of amphibian, halfway between existence and nonexistence.

Contemporary with Stevin was François Viète, an inadequately appreciated mathematician who likewise valued mathematical inutility. Trigonometry in its infancy had been so unfortunate as to be immediately applicable to astronomy and navigation, and hence, as a science of indirect measurement, it had had a limited growth. By subordinating the practical art of solving triangles to the liberal study of relationships among the trigonometric functions, Viète did much to convert the subject into a branch of pure mathematics, sometimes known as goniometry, or analytical trigonometry. Today in secondary schools the solution of triangles is giving way to increased emphasis upon the analytic side of trigonometry, and every electrical engineer, every student of optics and acoustics, knows through the work of Viète that the immediately practical is not in the end necessarily the most useful.

Descartes, Fermat, and Boyle

It is in the 17th century that one expects to see the other side of the coin—aspects of mathematics which were suggested by experience and which directly promoted the advance of science. Much of this there was, but less, I suspect, than is commonly assumed. Analytic geometry, for example, was not the practical outgrowth of a mundane use of coordinates. Descartes regarded his geometry as a triumph of philosophical method to be appreciated by the elite, and it took form in his mind as a generalization of an impractical locus problem inherited from ancient Greece. Apollonius had considered the locus of points for which the product of the distances to two of four given lines should be proportional to the product of the distances to the other two lines. Pappus had suggested, but was unable to complete, the generalization of this to six, eight, ten, or more lines, hinting at a geometry of more than three dimensions—the height of inutility, one should suppose. About this problem Descartes developed his coordinate geometry, the aim of which at the time was the theoretical geometric construction of the roots of equations that now would be solved by the practical man through successive arithmetical approximations.

Fermat, an independent inventor of analytic geometry, represents an even more striking instance of mathematical inutility, for he was as unconcerned about the practical outcome of his studies as he was about personal fame. And yet Fermat was an inventor in three branches which turned out to be among the most useful of all: he discovered the fundamental principle of analytic geometry; he invented the differential calculus; and he was a founder of the theory of probability. His coordinate geometry was scarcely more practical than Descartes'. It was a study of geometric loci, the "crowning point" of which was the following proposition: Given any number of fixed lines, the locus of a point from which the sum of the squares of the segments drawn from the point to meet the lines at given angles is constant is a solid locus (conic section).

Can this be used in the workaday world? His new infinitesimal analysis did turn out to have tremendous practical implications, but Fermat's thought here, too, was nonutilitarian. Perhaps the best way to describe his calculus is to say that it represented the first satisfactory definition of the tangent to a curve, a bit of theory which Newton and Leibniz developed into an algorithm which made possible the celestial mechanics upon which our hopes for space travel are founded. Even Fermat's theory of numbers, at the time far removed from the market place, has not been entirely without applicability, for his studies in figurate numbers enter into statistics.

Francis Bacon, in his utopian Solomon's House, had valued mathematics solely for its utility, but Robert Boyle, Fermat's Baconian contemporary, put in a good word for mathematical inutility. Boyle realized with regret that in mathematics one cannot in old age atone for the sins of neglect in one's youth, and it was not lack of training in practical mathematics that he regretted. "I confess," he wrote (*3*), "that after I began . . . to discern how useful mathematicks may be made to physicks, I have often wished that I had employed about the *speculative* part of geometry, and the cultivation of the *specious* Algebra . . . a good part of that time and industry, that I had spent about surveying and fortification . . . and other parts of *practick* mathematics" (italics mine).

The *Principia* of Newton probably never would have been written had it not been for the work of Fermat and others like him, and hence it can be regarded as the fruit of earlier mathematical inutility rather than as an inevitable outgrowth from social and economic roots of the time. In fact, there is not so large a proportion of applied mathematics in the book as is commonly supposed. Moreover, the philosophical import of the law of gravitation far transcended any practical significance. It should be noted also that Newton's contribution in this connection was not so much a discovery—some half a dozen men earlier had suggested an inverse square law—as it was a mathematical proof of the validity of the law, and the practical man has no truck with mathematical demonstration. Newton derived as a corollary of the law of gravitation the fact that within the earth the force

varies directly as the distance from the center—a bit of knowledge which at the time served no useful end but which carried within it the germs of potential theory and paved the way for the electromagnetic age.

In Time of Crisis

It is in times of crisis akin to our own that the temptation to undervalue mathematical inutility is great, but mathematicians of stature generally have risen above this. Few more striking instances of this can be found than during the French Revolution. Lazare Carnot and Gaspard Monge were key figures in the frantic defense against foreign invasion, yet during the turmoil they did not yield to the exigencies of the moment and divert their efforts to applied mathematics alone. Both men spent much time reviving pure geometry, one of the more beautiful but less immediately useful branches, and their names still are associated with theorems in the subject. Carnot, the "Organizer of Victory," wrote an especially useless work—one on the metaphysics of the calculus, which has gone through many editions down to our time—and Monge was instrumental in the establishment of the École Polytechnique, an institution which might well be taken as a model of balance between pure and applied mathematics.

Lagrange, one of the teachers at the school, spent much of his time looking for a logical foundation for the calculus—a pursuit which scientists of the time regarded as misdirected effort, but which has since led to the theory of functions, a subject which physicists find indispensable. But the theory of functions owed even more to what at the time looked like a fruitless effort. During the Napoleonic era no less than three men were toying with the idea of picturing imaginary numbers, and the result, now known as the Argand or Wessel or Gaussian diagram, became the basis for the theory of functions of a complex variable, with striking consequences for science. It probably is not too much to say that electrodynamics is the gift of the imaginary number, once shunned as useless.

Nineteenth Century Developments

Most ages have produced men who studied mathematics with little regard for its applicability, but the 19th century was a veritable paradise of mathematical inutility. One of the amazing things about this penchant of the century is that it proceeded in the main from *anciens élèves* of the École Polytechnique, a school of technology. In France, pupils of Monge stirred a revival in pure geometry such as had not been seen since the days of Apollonius. Projective geometry, with its concern for ideal elements, and the analytic geometry of imaginary points fascinated the heirs of the French Revolution, inapplicable though these studies might be. Poncelet, an engineer in the French army under Napoleon, reached the epitome of mathematical inutility when he noted that all circles in a given plane have two points in common—not ordinary points, of course, but two points which are both imaginary and at infinity! The two chief mathematical journals of the time both carried in the title the phrase (one in French, the other in German) "Pure and Applied Mathematics," but so obvious was the preponderance of pure mathematics that wags read the title as "Pure Unapplied Mathematics." And treatises of the time showed the same tendency.

The imaginary appeared everywhere in analysis, geometry, and algebra, and especially in the works of Cauchy. And what was the effect upon science of this feast of uselessness? It probably is safe to say that physics, at least, never developed more rapidly than during and immediately following the period we have been describing. Mechanics, optics, thermotics, acoustics felt the effect of Cauchy's theory of functions of a complex variable. But how, one may be inclined to ask, can the theory of the imaginary number have anything to do with the real world? The answer, of course, is that imaginary numbers are not fictitious, despite their name. What one generation labels impossible, another reduces to common sense. After Gauss, Wessel, and Argand had shown that imaginary numbers can be pictured as points in a plane, it was a short step to Sir William Rowan Hamilton's identification of the theory of complex numbers with the properties of couples of real numbers. This led Hamilton to devise a four-dimensional analog—the system of quaternions—and this in turn was later generalized into the theory of tensors, without which the mathematical theory of relativity would be unthinkable.

Relativity is in a real sense a bequest to science of once-useless mathematics. Not only is it an outcome of the imaginary number; it resulted also from some impossible geometries. Gauss, greatest mathematician of all times, played indifferently with useful and useless mathematics. His contributions in probability and statistics found ready application; much of his theory of numbers, which he enjoyed most, still is without palpable use. Among the mathematical toys of Gauss was one called non-Euclidean geometry, of which similar schemes were developed independently by Bolyai and Lobachevski.

The new geometries seemed to be a denial of common sense, but disagreement with sense never has been, and we hope never will be, a bar to mathematical investigation. If it had been, the 19th century would not have pursued the study of geometries of more than three dimensions. As it turned out, both non-Euclidean geometry and multidimensional geometry are applicable to science in the theory of relativity. Bertrand Russell has said that Riemann is logically the immediate predecessor of Einstein, and one might add that Cayley's geometry of n-dimensions, developed in 1843 with no inkling of possible applicability, has since found a place in thermodynamics, applied chemistry, and statistical mechanics. Here in America the analysis of Gibbs once was termed a "hermaphrodite monster," but the monster soon was tamed and became the chemist's best friend. Perhaps even today's bizarre mathematics of transfinite numbers eventually may become a scientist's man Friday. Had Hamilton been dissuaded on utilitarian grounds from toying with economically worthless noncommutative algebras, much of the abstract algebra of the 20th century would never have developed, and quantum mechanics would have been the loser.

The history of science seems indeed to support the findings of psychology in the thesis of a great nonagenarian mathematician of our day, Jacques Hadamard, who, on the basis of a study of *The Psychology of Invention in the Mathematical Field* (*4*), concluded that "practical application is found by not looking for it, and one can say that the whole of civilization rests on that principle."

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1. G. H. Hardy, *A Mathematician's Apology* (1941), pp. 59–60, 90.
2. L. Hogben, *Mathematics for the Million* (1937), p. 36.
3. R. Boyle, *Works* (London, 1772), vol. 3, p. 426.
4. J. Hadamard, *The Psychology of Invention in the Mathematical Field* (1945), p. 124.

News of Science

More Seismic Research Asked to Improve Atomic Test Detection

The text of a report by the Science Advisory Committee's panel on seismic improvement is published below. The report, which is expected to influence the Geneva negotiations on a nuclear test ban, was released 12 June.

The term decoupling, *as used in the report, pertains to techniques which prevent transfer to the surrounding earth of some of the energy released in the course of an underground explosion, resulting in inaccurate seismological recording of the event.*

The panel on seismic improvement, a group of distinguished American scientists under the chairmanship of Lloyd Berkner, president of Associated Universities, has recently completed a series of studies on the feasibility of improving the capability of the system recommended by the Geneva Conference of Experts last summer to detect and identify underground events.

The panel was appointed by the special assistant to the president for science and technology at the request of the State Department when it became apparent, from the analysis of new data obtained from the underground tests in Hardtack II last fall, that the capability of the Geneva System against underground tests was considerably less than had been originally estimated by the Geneva Conference of Experts.

The studies undertaken by the panel were directed at three basic problem areas: (i) the possibility of improving the Geneva System within existing technology; (ii) the possibility of further improving the Geneva System through a program of research in seismology; and (iii) the possibility that the capability of the Geneva System might be reduced by the concealment of underground tests.

The following analysis, prepared in consultation with the chairman of the panel, summarizes all of the conclusions contained in the studies by the panel on seismic improvement.

Earlier Report Cited

In order to interpret the conclusions of the panel on seismic improvement, it should be recalled that the Geneva Conference of Experts last summer concluded that, although it was not possible to identify an underground explosion by seismic means alone, it would be possible to identify a large fraction of seismic events as natural earthquakes when the direction of first motion of the seismic signal was observed at several, appropriately located stations. This procedure reduces the number of seismic events which would be unidentified and, therefore, could be suspected of being underground tests.

As was reported in the statement of the President's Science Advisory Committee on 5 January 1959, the analysis of later data from the underground tests at Hardtack last fall indicated that this method of distinguishing earthquakes from explosions was less effective than had been estimated. In addition, it developed that there were about twice as many natural earthquakes equivalent to an underground explosion of a given yield as had been earlier estimated.

These two factors meant that there would be a substantial increase in the number of earthquakes that could not be distinguished from underground nuclear explosions by seismic means alone. For example, the Geneva net of 180 stations, without modification, would have about the same capability (in terms of numbers of unidentified events) for seismic events above twenty kilotons equivalent as was originally estimated by the Geneva Conference of Experts for seismic events above five kilotons.

More Meters Needed

In considering the existing state of technology, the panel on seismic improvement concluded, with improved equipment and techniques that can be specified today, the Geneva net of 180 stations would acquire the same capability (in terms of numbers of unidentified events) for seismic events above ten kilotons equivalent as was originally estimated by the Geneva Conference of Experts for seismic events above five kilotons equivalent.

This partial recovery of the originally estimated capabilities of the Geneva System depends upon the incorporation of two improvements into the system.

The first improvement would increase the number of seismometers in the arrays at each station from 10 to 100, which would increase the ability of the system to distinguish "first motion" by reducing background "noise." On the basis of recent experiments, this improvement will increase the ability of the array to distinguish first motion by a factor of 2.5 over background noise.

The second improvement adds a new criteria for identifying natural earthquakes by means of the analysis of long period surface waves. An analysis of the Love waves (horizontally polarized surface waves) from five earthquakes similar in magnitude, direction, and distance to the Logan and Blanca nuclear shots indicated that the peak frequency in the explosions was twice that for earthquakes.

Another study of experimental data on the ratio of Love waves to Rayleigh waves (vertically polarized surface waves) and on the relative amplitude of surface waves and the *P* waves (used to determine first motion) also showed diagnostic possibilities to distinguish earthquakes from explosions. This experimental evidence led the panel to conclude that the analysis of long period surface waves can probably identify about 50 percent of earthquakes equivalent to five kilotons or more.

Data Limited

Table 1 compares the capabilities of the Geneva System, as initially estimated at Geneva last summer, with the estimates of the degradation of the system made in the light of data from the Hardtack tests and with the new estimates by the panel on seismic improvements that are now technically feasible.

In presenting these estimates, together with its other conclusions, the panel emphasized the limited nature of the data on which all estimates of seismic detection capabilities depend. There have been only a few underground nuclear shots; and all of these have been in the

same type of rock, and in a single geographical location. The type of rock, location, and shot chamber design can all have major effects on the strength of the seismic waves produced by a test of a given yield. The degree of coupling to the seismic waves achieved in the Rainier shot is the standard to which all estimates are adjusted.

Many Methods Promising

The panel concluded that a vigorous research program in seismology would result in important improvements in the ability to detect and identify earthquakes of small magnitude. Specifically, the panel believed that the program of research it recommended would in three years probably result in further improvements which could achieve the same capability in the Geneva net of 180 stations as was originally estimated by the Geneva Conference of Experts.

The panel submitted a very detailed technical report on the requirements for such a research program which will be published in the near future by the Department of State. Of the many ideas advanced by the panel, one of particular promise is the so-called "deep-hole" technique. There is evidence that the "background noise" which interferes with the detection of "first motion" is for the most part transmitted along the earth's surface. Therefore, seismometers located in holes thousands of feet below the earth's surface may be able to detect "first motion" with much greater sensitivity than instruments on the surface.

Another method of particular interest exists in the possibility of developing techniques to reconstruct the initial shock motion of an event from the seriously distorted and complex seismic waves observed at a distance. It may be possible to achieve this through the use of computer techniques which compensate for the passage of the seismic wave through the earth in such a way as to remove the distortions introduced.

The panel noted more generally that experience in analogous scientific fields suggests that vigorous research in the comparatively neglected field of seismology is likely to produce new ideas or approaches which will make additional large improvements possible.

Unmanned Stations Needed

The panel concluded that, in addition to the improvements discussed above, the augmentation of the Geneva net with an auxiliary network of unmanned seismic stations offers the possibility of major improvement in the capability to discriminate between earthquakes and explosions.

For example, if such unmanned stations were spaced at 170 kilometer intervals in and adjacent to the seismic areas of the world, about 98 percent of the events as small as one kiloton equivalent, located within the network, would be identified by this system. This capability would be reduced to about 75 percent for events located at the peripheries of continents. The capability of such a net would depend primarily upon the degree of reliability of equipment that could be achieved.

Some Nuclear Shots Necessary

All of the above estimates by the panel refer to nuclear explosions conducted under conditions similar to those of Rainier, Logan, and Blanca in the Nevada test sites. The panel concluded that, although the differences in seismic signals from shots conducted in different geological environments cannot be predicted with any certainty, it is entirely possible that some natural conditions will yield seismic signals much smaller for a given size shot than those from shots in the volcanic rock at the Nevada test site.

The panel recommended that, in order to resolve the uncertainty on this question, an experimental test program involving many high explosive and some nuclear shots should be undertaken as soon as feasible.

Decoupling Can Mask Shots

In considering the possibility that the capabilities, now or in the future, of the Geneva System might be reduced by the intentional concealment of underground tests, the panel concluded that decoupling techniques existed which could reduce the seismic signal by a factor of ten or more. Moreover, preliminary theoretical studies have shown that it is possible in principle to reduce the seismic signal from an explosion by a much greater factor than this.

Nevertheless, in view of the many complexities involved, it is necessary that these ideas be tested with appropriately designed experiments to determine how large a decoupling factor can actually be realized in practice.

While many of these tests can be carried out with high explosives, complete evaluation of the theory probably cannot be made without nuclear explosions. Such tests may also disclose some characteristics which might allow long-range detection of such decoupled underground tests.

Table 1. Estimated annual number of unidentified world-wide continental earthquakes.

	5 Kilotons and greater	10 Kilotons and greater	20 Kilotons and greater
Geneva Conference of Experts, Aug. 1958	20–100		
Geneva network and equipment on basis of Hardtack data Jan. 1959	20–100	400	60
Geneva network with improvements within the present state of technology on basis of Hardtack data April 1959	300	40	15

Prototype Station

The panel emphasized the need to construct a complete prototype experimental station incorporating all features of the seismic stations recommended by the Geneva Conference of Experts.

Operating this station for a period of time would serve the two immediate objectives of providing experimental evidence on the capability of such stations to detect and identify earthquakes, and of assisting in working out installation and operational problems which would be encountered in establishing a control network. Subsequently, the station should be expanded to include facilities for testing other detection methods proposed by the panel or methods which may be developed through future research programs.

Panel Members

The following scientists, representing the fields of seismology, geophysics, electronics, physics, and mathematics, were members of the panel: Lloyd Berkner, Associated Universities, Inc., chairman; Hugo Benioff, California Institute of Technology; Hans A. Bethe, Cornell University; W. Maurice Ewing, Columbia University; John Gerrard, Texas Instruments, Inc.; David T. Griggs, University of California at Los Angeles; Jack H. Hamilton, the Geotechnical Corporation; Julius P. Molnar, Sandia Corporation; Walter H. Munk, Scripps Institute of Oceanography; Jack E. Oliver, Co-

lumbia University; Frank Press, California Institute of Technology; Carl F. Romney, Department of Defense; Kenneth Street, Jr., Lawrence Radiation Laboratory, University of California; John W. Tukey, Princeton University.

In addition, Warren Heckrotte, Lawrence Radiation Laboratory, Montgomery Johnson, Aeronutronic Systems, Inc., and Albert Latter, Rand Corporation, participated as special consultants to the panel.

Strauss Rejected as Commerce Secretary by Senate

Voting half an hour after midnight, 19 June, the United States Senate rejected by three votes the nomination of Lewis L. Strauss as Secretary of Commerce. The Senate action, which climaxed three months of growing controversy over the issue, represents the first rejection of a Cabinet appointee since 1925. Strauss, who was defeated by a 49 to 46 vote, is the eighth such nominee to be refused confirmation in the history of the country. He had been Acting Secretary of Commerce since his appointment by President Eisenhower last fall. Under the Constitution, the President's appointments must be made with the advice and consent of the Senate. After committee hearings on the nomination, which produced 1100 pages of testimony, Strauss' name went to the full Senate after approval by a narrow margin. Floor debate produced little new information, and the issue was pushed to a conclusion by Senate majority leader Lyndon Johnson (D-Tex.).

The course of events in the Strauss controversy represented a steady downward progression of the nominee's prospects. When the first confirmation hearings before the Interstate and Foreign Commerce Committee convened, 17 March, an informal poll showed the committee members to be 14 to 3 in favor of confirmation. As the sessions continued, the positions of many of the members changed, with the result that the final committee vote was a close 9 to 8 for confirmation. When the nomination came up for consideration by the full Senate, the general opinion in Washington was that Strauss would make it. However, very effective opposition, led by Senator Clinton Anderson (D-N.M.), and the negative position taken by the Senate majority leader, among other factors, resulted in Strauss' rejection.

Number of Foreign Scholars in U.S. Increases

The number of foreign students studying in the United States has increased by 38 percent in the last five years, the Institute of International Education has reported. The 47,245 students from 131 countries registered in U.S. colleges and universities this year represent a 9-percent increase over the number last year and an 86-percent increase over that of the academic year 1948–49. According to all available statistics the current figure represents the largest foreign-student population in any country of the world.

The postwar period has also produced a great increase in the exchange of university teachers and scholars, the institute reported in its 1959 edition of *Open Doors,* an annual statistical report on educational exchange. In 5 years, the number of foreign professors teaching in our schools has tripled. American colleges and universities reported 1937 foreign faculty members this year, in comparison to 635 in 1954–55. This was the first year on record that the United States, with 1842 American faculty members abroad, "imported" more professors than it "exported."

The sharp increase in both the "export" and "import" figures reflected the United States' growing concern with education in the physical sciences. Nine hundred and seven, or 47 percent, of the foreign professors brought to American schools this year were in this field. This was double the number of foreign science professors brought here last year. The number of American science professors who went abroad to teach and to do research was 389—43 percent more than last year.

"The increasing percentage of foreign students attracted by our science courses seems to show that the United States is achieving new status in science education," said IIE president Kenneth Holland in commenting on the survey.

The rapidly developing Middle East sent a record number of students here this year, according to *Open Doors.* This was the first year that more students came from the Middle East than from Europe to study in the United States. The largest number of foreign students (15,823) continued to come from the Far East, and the second largest number (10,249), from Latin America. The Middle East was third, with 6619, and Europe fourth, with 6601. Engineering, which claimed 23 percent of the students, continued to be the most popular field of study. The humanities, with 20 percent, was again second. Students from the Far East, the Middle East, and Latin America, concerned with the industrialization of their respective countries, again concentrated on engineering courses. Many of the new students in the physical sciences were also from the Far and Middle East.

Statistics on sources of financial support showed that, again this year, students who made up the largest single group (42 percent) supplied their own funds. Those in the next largest group (28 percent) were aided by scholarships from private organizations. There was a slight increase this year in the number of students supported by foreign governments; a particularly large number of African students received help from their own governments. The United States government gave scholarship aid to 4.8 percent of all students and joined with private organizations in supporting another 2 percent. These statistics again point up the vital role of private foundations and fraternal and civic organizations in bringing foreign students to our shores and also seem to indicate that the prestige of our schools is as much a factor in attracting students as the availability of scholarships.

Another reason for the influx of foreign students to this country was indicated by the large number who said they would welcome employment with the overseas branch of an American firm after graduation. Forty-one percent of the students answering the pertinent question in the survey expressed such an interest. More than half of these were engineering students, a third of them from the Far East.

The University of California was again the institution with the largest number of foreign students. Massachusetts Institute of Technology, however, had the highest percentage of foreign students—12 percent of its total enrollment. Massachusetts Institute of Technology also had more foreign faculty members (198) than any other United States college or university.

Archeological Work in Guatemala

An expedition from the University of Pennsylvania Museum has completed its fourth season of work at the ancient Maya site of Tikal, located near the center of the tropical rain forests of the Yucatan Peninsula's El Peten region in

northern Guatemala. The site is being explored and partially restored by the museum archeologists in cooperation with the Guatemalan government. The most important single discovery this year was that of the oldest known dated stone monument of the lowland Maya tribes. Clearly legible inscriptions on the weathered and fragmentary piece give a date which, by one correlation of the Mayan and Christian calendars, corresponds to A.D. 32 and, by another correlation, to A.D. 292. Regardless of which of these dates is used, the stela is 36 years older than the archeologically famous Stela 9, discovered at Uaxactun, Guatemala, in 1916 by the Carnegie Institution of Washington, D.C., and 28 years older than the jade plaque, known as the Leyden Plate, which was found near Puerto Barrios, Guatemala, in 1864. Archeologists have theorized, on stylistic grounds, that the Leyden Plate, although it was not found at Tikal, was produced there, because of its resemblance to other stone carvings from the same city.

Automatic Weather Station

A new automatic "weather bureau" that can be set up anywhere in the world as a complete, unattended observatory supplying key data to a central office has been designed and built for the U.S. Army.

The weather station, a steel cubicle 7 by 7 by 8 feet and weighing less than a ton, is equipped to report by teletype code, in 15 seconds, its identification; the air temperature, from minus 40° to plus 120°F; the dew point temperature; the wind direction and velocity; and the barometric pressure and rainfall. It can also be equipped with radiation monitoring and warning instruments.

The new unit is a compact, transportable, automatic meteorological station, designed to operate unattended and automatically, taking observations and reporting data over wire or radio facilities to any central location, either on demand or at prescribed intervals, as desired. There is no limit to the number of stations that may be combined to form a world-wide weather observation network.

The new equipment, by eliminating the need for human supervision, makes possible a major expansion of world-wide meteorological observation and forecasting at minimum cost and eliminates the need for personnel to be stationed in remote locations.

News Briefs

The Public Health Service reported in June on the levels of radioactivity in milk collected during March from 12 sampling stations across the country. According to the report, the averages for all radioisotopes in the milk samples remained below the levels which the National Committee on Radiation Protection and Measurements currently suggests as permissible for the general population.

The milk-sampling network is part of the service's program of measurement of radioactivity in air, water, and food. Milk was chosen for the initial study of specific isotopes in foods because it is the easiest of all foods to sample and is produced throughout the year in all sections of the country.

* * *

The world's largest installation for distilling fresh water from sea water has recently been completed, at a cost of $10,600,000. The plant is located on the island of Aruba in the Netherlands West Indies, off the coast of Venezuela. Electricity is produced by a by-product of the water distillation plant, at a cost of less than 3 mills per kilowatt hour, it was reported.

* * *

Devices which generate electric power directly from heat, without the use of boilers and spinning generators, were described at a meeting of the American Society of Mechanical Engineers in St. Louis last month. One such device, called a fuel cell, would burn conventional fuels to produce a flow of usable current. The other, called a thermionic converter, might use heat from a nuclear reactor or from the rays of the sun.

In a fuel cell, a fuel such as hydrogen, coal, or carbon monoxide reacts with oxygen from the air. Instead of heat, this reaction generates electricity directly. In its simplest form, a thermionic converter consists of a vacuum tube in which one piece of wire is heated until it gives off electrons, while another, colder, piece collects the electrons and feeds them to an outside circuit.

* * *

The Marine Biological Association of India was founded in January, with S. Jones as president. The association expects to issue a journal half-yearly. Membership is open to all interested. Correspondence may be addressed to the Secretary, Marine Biological Association of India, Marine Fisheries P.O., Mandapam Camp, South India.

Scientists in the News

Sir HARRY MELVILLE, secretary of Department of Scientific and Industrial Research, London, will arrive in the United States on 24 August. He will visit Washington (25–28 August); Kingsport, Tenn.; Ottawa, Canada. On 2 September he will attend the Faraday Society meeting in Kingston, Ontario, Canada.

B. J. RENDLE, principal scientific officer, Forest Products Research Laboratory, Princes Risborough, Aylesbury, England, will arrive on 19 July. He will attend the Northeastern Forest Tree Improvement Conference, Burlington, Vt., 18–19 August, and the ninth International Botanical Congress, Montreal, Canada, in August. His itinerary includes Connecticut; New York; Wisconsin; Vancouver, B.C.; Ottawa; and Chalk River, Ont.

HENRY L. BOCKUS, professor and chairman of the department of medicine at the University of Pennsylvania Graduate School of Medicine for 30 years, retired on 1 July. Former graduate students presented a portrait of Bockus to the university at the first annual meeting of the Bockus International Alumni Society of Gastroenterology, which was organized last year in his honor. At the group's first banquet, attended by 180 physicians from the United States, Europe, Africa, the Near and Far East, and Latin America, Bockus was given a specially designed map of the world that showed the location of the 325 gastroenterologist alumni of his program.

EDWARD C. WENTE, scientific staff member of Bell Telephone Laboratories until his retirement in 1954, and pioneer inventor of important devices for the motion picture, recording, broadcasting, and television industries, has been awarded the Gold Medal of the Acoustical Society of America.

LILLIAN M. GILBRETH, engineer and former chairman of the department of personnel relations at Newark College of Engineering, has received the Allan R. Cullimore Medal. The medal was established last year in memory of Dr. Cullimore, NCE's first president.

MURRAY KORNFELD, founder and executive director of the American College of Chest Physicians, received the college's Gold Medal during its recent

25th anniversary meeting in Atlantic City, N.J. The first layman to receive the medal, Kornfeld was honored for "having devoted 32 years of his life as a leader in furthering the specialty of diseases of the chest."

ANTON B. BURG, professor of chemistry at the University of Southern California, will give a 1-hour lecture at the 17th Congress of Pure and Applied Chemistry, in Munich, Germany, next September. His subject will be "Chemical Behavior and Bonding of Boron-Hydride Derivatives."

GERTRUDE M. COX, director of the Consolidated University of North Carolina's Institute of Statistics, at North Carolina State College, has been named the 1959 winner of the Oliver Max Gardner Award for having made "the greatest contribution to the welfare of the human race" during the current academic year.

EMERY I. VALKO, professor of chemistry in the Lowell Technological Institute's division of chemistry, has received the 1959 Olney Medal of the American Association of Textile Chemists and Colorists.

A. M. SCHLEHUBER, professor of agronomy at Oklahoma State University, will be on sabbatical leave at the Technical Institute, Munich, Germany, during the academic year 1959–60. He will lecture on plant breeding.

S. E. A. McCALLAN, plant pathologist at the Boyce Thompson Institute for Plant Research, Yonkers, N.Y., and a staff member for 30 years, has been appointed secretary of the institute. He succeeds JOHN M. ARTHUR, who will retire after 38 years of service.

ALFRED A. H. KEIL, physicist and chief scientist of the Underwater Explosions Research Division at the Norfolk Naval Shipyard, has been appointed technical director of the Structural Mechanics Laboratory at the Navy's David Taylor Model Basin, Washington, D.C.

BRUCE L. DOUGLAS, chairman of the editorial board of the American Dental Society of Anesthesiology and diplomate of the American Board of Oral Surgery, is going to Japan for a year to teach oral surgery and anesthesiology at Okayama University Medical School.

JOHN S. KARLING, head of the department of biological sciences, director of the Ross Biological Reserve, and professor of botany at Purdue University, was named Distinguished Professor during the university's recent commencement exercises. He will occupy the John Wright chair of biological sciences and devote himself to teaching and research in the development, physiology, and systematics of fungi.

DOUGLAS D. BOND, professor of psychiatry at Western Reserve University and director of the division in the university hospitals, has been appointed dean of the School of Medicine. He succeeds JOSEPH T. WEARN, who has been appointed to the newly created post of vice president for medical affairs.

RONALD C. VICKERY, formerly with the Stanford Research Institute, has been named senior research scientist of the Research Chemicals Division of the Nuclear Corporation, Burbank, Calif. Vickery is a specialist in rare earth elements.

JOHN H. GARLOCK, clinical professor of surgery at the College of Physicians and Surgeons of Columbia University, has been named a governor of the Hebrew University, Israel.

RUDOLF E. A. THUN, physicist, has received the Commanding General's Medal for Technological Achievement, one of the highest awards that can be conferred upon an employee at the U.S. Army Engineer Research and Development Laboratories, Ford Belvoir, Va.

DALE H. SIELING, dean of the University of Massachusetts College of Agriculture, has been appointed scientific director of the U.S. Army Quartermaster Research and Engineering Command, Natick, Mass.

FRED R. JONES, who retired in 1958 as head of the agricultural engineering department at the Agricultural and Mechanical College of Texas, received the John Deere Gold Medal of the American Society of Agricultural Engineers at its special awards program at Cornell University on 25 June.

FLOYD W. DUFFEE, chairman of the agricultural engineering department at the University of Wisconsin, received the society's Cyrus Hall McCormick Gold Medal on the same occasion.

Recent Deaths

JOHN P. DEAN, Ithaca, N.Y.; 45; associate professor of sociology and anthropology at Cornell University; 31 May.

CHARLES F. DEISS, Indianapolis, Ind.; 56; chairman of the Indiana University department of geology and Indiana state geologist; formerly taught at Montana State University; 13 June.

HARVEY L. FULLER, Atlantic City, N.J.; 44; specialist in internal medicine and staff member at Sinai Hospital and the University of Maryland Hospital; conducted research on heparin, a drug that dissolves fatty deposits in the body that contribute to narrowing of arteries; 9 June.

RALPH K. GHORMLEY, Rochester, Minn.; 66; orthopedic surgery consultant to the U.S. Veterans Administration; head of orthopedic surgery at the Mayo Clinic, 1938–55; coauthor of *Diagnosis in Joint Diseases*; 6 June.

LUDLOW GRISCOM, Mass.; 68; research ornithologist, research curator, and editor at the Harvard Museum of Comparative Zoology from 1927 until his retirement in 1955; assistant curator in ornithology at the American Museum of Natural History, 1921–27; president of the American Ornithologists Union in 1956; author of *Birds of Martha's Vineyard*; 28 May.

MORTON C. KAHN, New York; 63; explorer, bacteriologist, and public health specialist; chief bacteriologist at St. Vincent's Hospital since 1955; associate professor of public health and preventive medicine at Cornell University Medical College, 1934–55; former head of the department of parasitology of the New York Hospital; recently had been conducting experiments on the resistant staphylococcus bacteria; made field trips to Costa Rica, Honduras, the Gold Coast, and British and Dutch Guiana; 6 June.

WILLIAM H. W. KNIPE, Katonah, N.Y.; 78; practiced gynecology and obstetrics from 1906 until his retirement last April; studied the techniques of twilight sleep in Germany, and introduced it in this country in 1914; 28 May.

ADOLF WINDAUS, Goettingen, Germany; 82; professor of applied medical chemistry of the University of Goettingen from 1915 until his retirement in 1944; received the Nobel Prize in 1928 for research which demonstrated that the substance ergosterol could be converted to vitamin D; 9 June.

Book Reviews

Handbook of Physics. Prepared by a staff of specialists. E. U. Condon and Hugh Odishaw, Eds. McGraw-Hill, New York, 1958. xxvi + 1504 pp. Illus. $25.

This work compresses into a single volume a tremendous wealth of information. Some idea of the scope of the book can be obtained from a listing of the nine parts into which it is divided. These parts are: "Mathematics," "Mechanics of particles and rigid bodies," "Mechanics of deformable bodies," "Electricity and magnetism," "Heat and thermodynamics," "Optics," "Atomic physics," "The solid state," and "Nuclear physics." Each part contains a series of chapters on the major topics pertaining to the main subject. For example, under "Mathematics" there are chapters on arithmetic, algebra, analysis, ordinary differential equations, partial differential equations, integral equations, operators, geometry, vector analysis, tensor calculus, calculus of variations, elements of probability, and statistical design of experiments, while under "The solid state" there are chapters on crystallography and x-ray diffraction, the energy-band theory of solids, ionic crystals, flow of electrons and holes in semiconductors, photoelectric effect, thermionic emission, glass, and phase transformations in solids. There is an average of ten chapters in each part. The various chapters are written by experts in the subjects discussed.

A notable feature of modern science is its rapid rate of advancement. As a result, written works on the newer aspects of a subject such as physics become out of date with dismaying rapidity. A reference work, in particular, runs into difficulties here, since those who consult the work will quite often be seeking information about the latest findings and concepts. The attempt to meet this demand must have posed difficult problems for the editors of the *Handbook of Physics,* since preparation of the work, from first planning to completion, took nearly 10 years. Nevertheless, the editors state that an effort was made to have the book as up to date as possible at the time of publication. They appear to have been reasonably successful in this effort.

I examined the *Handbook of Physics* from two points of view, evaluating it first as a reference book and second, as a text (or rather series of texts) for self-instruction. As a reference, this handbook should be very useful. It contains a wealth of material, including much that is recent. The organization of the material is excellent, and the writing is good. The typography is clear and pleasing.

One result of the effort to cover an extremely wide range of topics in a single volume is a compactness of treatment that makes reading difficult. Occasionally the treatment is so compact as to be uninformative. Because of the concise treatment, the *Handbook of Physics* appears to be designed more for the professional physicist than for use as a general reference work.

A most important part of a reference book or handbook is its index. It is here that I found the principal weakness in the *Handbook.* The indexing is incomplete. In making a sample check list of items, I found a tendency to omit the indexing of simple definitions. There is little cross-referencing or multiple-listing when several different terms or phrases are commonly used for the same subject.

To summarize, as a reference work, the *Handbook of Physics* is a useful and clearly but compactly written volume. It is reasonably up to date and covers a wide range of topics in classical and modern physics. It is intended more for the professional physicist than for general reference. Its index would be improved by enlargement and extensive cross-referencing.

Since the *Handbook* covers such a wide area in the field of physics, I found it of interest to consider whether or not it could be used as a text for self-instruction. The compactness of the writing appears to limit the book's usefulness for this purpose. On the other hand, the various chapters provide splendid summaries in their respective areas and can be used for self-instruction in conjunction with the texts and articles listed in the bibliographies at the ends of the chapters. Many of the individual chapters, expanded to book size, would make excellent texts. It might be worth while for individual authors to consider this possibility.

Finally, the *Handbook* is doubtless the best existing compromise between the brief type handbooks available and multivolume sets, such as the *Handbuch der Physik.*

HOMER E. NEWELL, JR.
National Aeronautics and Space Administration

The Way Things Are. P. W. Bridgman. Harvard University Press, Cambridge, Mass., 1959. x + 333 pp. $5.75.

The readers of Bridgman's earlier writings will find in this, his latest book, a clearer and more systematic presentation of his "operational methodology." By this he means simply that an analysis of what we know in terms of doings or happenings is preferable to one in terms of objects or static abstractions. Three aspects of his position, heretofore more or less implicit, have now become abundantly clear.

First, analysis merely in terms of physical operations is insufficient; physiological operations must also be brought into the picture. "Not only should we never think of the microscopic world without thinking of microscopes, but we should never think of the microscopic world without thinking of ourselves using the microscope" (page 154). By "ourselves" he means "the nervous machinery in our heads." In the second place, to describe this physiological contribution of the knower in objective, behavioristic terms, as many psychologists do, is not adequate; introspectional language has a legitimate, though somewhat restricted, use. For example, the operation by which I determine that *I* have a toothache is quite different from the operation by which I determine that *you* have a toothache. This distinction, says Bridgman, is so sharp and spectacular that it must never be forgotten. Finally, the most desirable description of any analysis is one given in the first person;

for the investigator cannot get away from the fact that it is he himself who is knowing something, and *what* he knows is often in very significant ways determined by this fact.

Within this framework Bridgman presents interesting, and often very penetrating, analyses of logic, physics, psychology, and the social sciences. Perhaps the most important point which he uncovers by these considerations is that as we pass from the abstractions of logic to the value judgments of the social sciences, the role of the individual knower becomes increasingly important. Although it is true that when I utter a proposition of Euclid I must consider the fact that I am uttering it as part of the total picture, this is not nearly so significant as when I state a truth about society. For here I must recognize that there are no "values" (without qualification) but only "values-for-someone"—in this case, myself.

It may be worth while to point out that two of the most important of the recent schools of philosophy—the Existentialists and the Linguistic Analysts—also take their departure from the concrete individual. The former considers him as a creature experiencing anguish and dread; the latter, as a symbol-using animal endeavoring to communicate the simple truths of his experience. I hesitate to present Bridgman with such ill-deserved bedfellows. But there may be significance in the fact that intelligent people in widely different areas are deploring the modern overemphasis on abstraction, togetherness, and the "public interest," on the grounds that this may lead us, as individuals, unwittingly to commit suicide.

A. Cornelius Benjamin
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The Great Decision. The secret history of the atomic bomb. Michael Amrine. Putnam's, New York, 1959. 251 pp. $3.95.

This is a valuable and interestingly written contribution to a particular chapter of the history of atomic energy for military purposes. It begins with the afternoon of 12 April 1945, when Vice-President Harry Truman was informed by Eleanor Roosevelt of the death of the President.

That evening Harry Truman was sworn in as President of the United States. Later there was a brief cabinet meeting, and Secretary of War Henry L. Stimson lingered for a private word with the President. That was Truman's first official knowledge of the atomic bomb project, which at that moment had about 100,000 persons working in secret laboratories and factories. The great bulk of these persons were unaware of the over-all objective of the factories in which they worked.

This was just 116 days before the whole character of war was changed by Americans when they dropped one atomic bomb on Hiroshima, Japan. This was followed three days later, 9 August 1945, by the dropping of another bomb on Nagasaki, Japan. During the afternoon of 14 August the Emperor of Japan announced his acceptance of the terms for ending the war contained in the Potsdam Declaration, and World War II was at an end.

Michael Amrine has given a brilliant synthesis of the peculiar circumstances of those less-than-four momentous months in history. He has searched carefully and told the story as well as anyone could in view of the fact that not all of the essential information has been made public. He is aware of the incompleteness of his narrative, for he says in the concluding chapter: "We look back, with troubling questions, at these events, which helped so much to set new limits and choices for man. Were the atomic bombings necessary for an early end to the Pacific war? Were the atomic bombs used in haste, without proper thought of the consequences?

"This book was written to help people answer these questions for themselves. There is also a hope that if the available record is set down, as far as it can be, other people who have not yet spoken may tell the full story of their participation. There are official records that should be opened now. Some contain no official secrets. Others contain technical secrets now outmoded. It is time for these records to be opened, but, so far, the doors have remained shut to journalists, historians, and sometimes to former officials, even to famous American officials who lived through these events. A nation, like a man, cannot fully understand its future if it does not understand some of the secrets of the past."

As we begin to appreciate the vastness of the consequences of atomic energy with its million-fold multiplication of war's horrors which now threaten humanity, one of the most important tasks of scholarship becomes the writing of a really definitive history of atomic energy. This is not a project to be undertaken by one or two men: it calls for the coordinated efforts of a major group of physical scientists, social scientists, and historians. These scholars should subject the stories of the various groups to searching critical analysis so that men may know what a great change atomic energy has worked in every facet of their lives.

My part of the project was finished by February 1945 and, in any case, since I was never associated with it at a level that could influence policy, I have little first-hand knowledge of the story that Amrine gives us. But what I do know confirms the essential accuracy of the story as he tells it. It may be useful to point up some comments on the parts of the story which seem most significant.

A complete history would tell how the project was born in complete and equal cooperation between the United States and Great Britain. We did very little on the project between 1939 and the fall of 1941 while the British accomplished a great deal in spite of the distractions caused by the disaster at Dunkirk and the Germans' mass-bombing of English cities.

Our scientists were indecisive and ineffectual in this early period. It was mainly the push afforded by the British scientists which led to the organization of a major project in the late fall of 1941. At that time it was agreed that the British would shift their work to this country and that we and they would work together on the project as equal partners.

In 1942 General Leslie Groves was put in charge of the project. The full story has not yet been told of how he worked to hobble and frustrate this cooperation. Amrine mentions it briefly (pages 121–2). He tells how, by February 1943, Sir Winston Churchill's irritation reached such a point that he cabled Harry Hopkins the following message: "I should be very grateful for some news about this, as at present the American War Department is asking us to keep them informed of our experiments while refusing altogether any information about theirs."

By August 1943 this had become a major issue and was discussed at the Quebec Conference between Churchill and Roosevelt. After this it was no longer possible for Groves to frustrate cooperation with the British. It was not until that time—but it happened with great speed immediately thereafter—that a

large, able group of the best British scientists came to the United States to help in every phase of the project at the many different laboratories and factories.

It was about this time that Churchill, feeling that the Americans under General Groves were intent on "squeezing out" the British, made the "somber decision" to go it alone by setting up an independent effort at Chalk River, Canada. This conduct on our part which, in my judgment, was clearly aimed at hampering Britain's development of atomic energy for industrial purposes after the war, put a severe strain on Anglo-American cooperation.

Another topic that needs fuller exploration, as Amrine indicates, is the kind of specific detail about the bomb that was available to our policy makers at the time policy decisions on how to use the bomb were being made. Amrine tells us (page 132) that General Groves, in a memorandum to General George Marshall dated 30 December 1944, vastly underestimated the power of the bomb. He estimated the power of the bomb at only 500 tons of TNT, whereas it was actually 20,000 tons when used on Hiroshima. As Amrine says, our military planners "were only given reason to think it was a spectacular improvement in bombs, not another kind of warfare."

Now I know that General Groves did not know enough physics to make his own estimate; and I do not believe that anyone at Los Alamos would have made such a low estimate. How then could Groves have erred by a factor of 40? Could it have been intentional, so that the top policy planners would not be aware of the horribly serious nature of the decision they were taking?

It would have been quite easy to mislead the White House especially since Admiral Leahy—the staff military adviser, who "had had a long experience with explosives"—long thought the project a gigantic "boondoggle" because "this bomb did not fit anything he knew about explosives" (page 134).

Moreover, it would be natural for Leahy to discount the bomb because the thing, if a reality, horrified him. To use it, he believed, was to adopt "an ethical standard common to the barbarians of the Dark Ages. . . . I was not taught to make war in that fashion . . . these new and terrible instruments of uncivilized warfare represent a modern type of barbarism not worthy of Christian men" (page 170).

I believe that an erroneous view of the magnitude of their responsibility was planted in the minds of the nation's leaders by the 30 December 1944 memo of General Groves and that this erroneous view was not changed by the later, brief, coded messages. Truman learned of the Alamogordo test on 17 July by this message which was sent to him at the Potsdam Conference, "Babies satisfactorily born." This was certainly designed to minimize the seriousness of a new development of which the President had first become aware in sketchy outline just three busy months earlier.

At Potsdam it was decided that Truman should inform Stalin of the new weapon. We do not know exactly what he said when he did this. Truman has written (page 187), "On July 24 I casually mentioned to Stalin that we had a new weapon of unusual destructive force. The Russian Premier showed no special interest . . ."

But apparently, Truman had not used the key words "nuclear" or "atomic" and, perhaps because of the 30 December 1944 memo, may not have himself at that time fully realized the magnitude of the revolution in warfare that had occurred.

Amrine's account of this affair (page 190) is fascinating: "No one at Potsdam had time to think much about the lack of reaction from Stalin to the news. Perhaps they thought that (like Admiral Leahy) Stalin found it hard to believe in these superweapons." But had he really been told of a *super*weapon? "Perhaps, like James Byrnes, he found it hard to understand scientific matters."

The book tells in detail of the sustained efforts of the scientists on the project to get our government to give some kind of demonstration or warning to the Japanese before actually using the atomic bomb against them. It has often been said that the Potsdam Declaration met this minimal moral demand. But one may very well ask whether it really did so, when this is all that it said that might be so construed (page 191): "We call upon the government of Japan to proclaim now the unconditional surrender of all Japanese armed forces, and to provide proper and adequate assurances of their good faith in such action. The alternative for Japan is prompt and utter destruction."

The last chapter, "Conscience and questions," is a searching analysis of the troublesome questions that still perturb the thoughtful, about whether or not the bomb should have been used.

Because the entire attack on Hiroshima involved only three planes, the air raid alarm was not sounded and people did not take shelter. Amrine writes: "That accidental happening cost the lives of tens-of-thousands of women and children who were not military targets and whom we had no intention of killing" (page 229).

Amrine says that his "personal observation is that many Asians and Americans thought differently about Western man's supposed respect for human life. These bombs did not improve our reputation and win us allies in Asia" (page 233).

It is a sad story, one that many would like to forget or, if possible, never to learn. But it only involved two bombs of the type, now called conventional, which we stockpile by the hundreds or thousands and recklessly issue to our ally, West Germany, where "ex"-Nazis get greater political power day-by-day. In the meantime hydrogen bombs, which are a thousand times more powerful than the obsolescent toys of World War II, are in the hands of Americans, British, and Russians, and the means to deliver them half way around the world are being perfected by both sides.

Thus there is probably no exaggeration in the assertion by Congressman Charles O. Porter (D.-Ore.) in his May newsletter to his constituents when he says: "Two very prominent authorities, one on disarmament and the other on science, stated in my presence the other day their belief that we would all be dead in 10 years and that the earth would be an incinerated relic."

There is no doubt whatever that the technical means of achieving such a goal do exist at the present. Amrine's story of a few months in 1945 gives one a foretaste of how this larger catastrophe may come about, and not as a result of a free choice by the peoples of the world.

E. U. CONDON
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The Sociological Imagination. C. Wright Mills. Oxford University Press, New York, 1959. 234 pp. $6.

C. Wright Mills is caught up in the present-day dilemma of scientists: the "scientific" and the "moral" are obviously inextricable on the one hand, but on the other they are apparently at odds. Out of the depth of his feeling and the

breadth of his knowledge, he has written a fascinating but ultimately unsatisfactory book. He suggests that social scientists probably have done themselves the ultimate disfavor by linking themselves terminologically with the older sciences, and certainly have stultified themselves by analogies with the "natural" sciences. He also believes, and I agree, that the social-science attitude—which he calls the sociological imagination—is the pervading *Geist* of our age.

The first half of this book, in which Mills tries to get his own position straight, is a critique in broad strokes of some features of several of the foremost schools of sociology. He makes good cases, but unfortunately he writes in a style essentially popular about matter in which there is only specialist interest. The style will alienate rather than persuade his colleagues. At the same time, it is doubtful if the general reading public cares to be edified with denigration of the particularities of system building or opinion factoring.

The second half of the book explores Mills' thesis that the sociological imagination concerns itself with the converging points of history, biography, and society, and that it should distinguish *troubles* from *issues* and face the issues of modern society squarely. This section can be read as a clarion call for a successor to Max Weber.

Mills' romp through the theoretical fields is not as giddy or as enlightening as Sorokin's. His *engagement* is not as compelling as Raymond Aron's. And what he has to say is ill-matched with the way in which he chose to say it.

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Semiconductors. N. B. Hannay, Ed. Reinhold, New York; Chapman and Hall, London, 1959. xxiii + 767 pp. Illus. $15.

This volume is the most recent addition to the American Chemical Society's "Series of Chemical Monographs." Written and edited by 17 members of the technical staff of Bell Telephone Laboratories, the volume is a happy balance of chemistry, metallurgy, physics, and electronics and should prove useful to a wide circle of readers.

Essentially, the book is a collection of authoritative and up-to-date review articles on divers aspects of semiconductor physics and chemistry. The introductory article by the editor, N. B. Hannay, summarizes the basic concepts and principles of semiconductor physics. The article by J. J. Lander provides a survey of some of the problems of semiconductor chemistry; these are dealt with in more detail in subsequent sections.

The next five contributions are concerned with the physical chemistry of semiconductor systems: M. Tanenbaum discusses semiconductor crystal growing; C. D. Thurmond describes the control of composition in semiconductors by freezing methods; C. S. Fuller considers the theory of defect interactions; H. Reiss and C. S. Fuller discuss diffusion processes in germanium and silicon and illustrate the important advantages offered by semiconductors in general for the study of diffusion processes; and D. G. Thomas concludes this section by reviewing the chemistry of some compound semiconductors.

The eight articles that follow deal with the physical properties of various semiconductors. T. H. Geballe describes the progress that has been made in understanding the physical behavior of group IV semiconductors, while J. M. Whelan does the same for other covalent semiconductors, particularly group III–V, II–IV, and V–VI compounds, boron, selenium, and tellurium.

H. J. Hrostowski discusses infrared absorption and demonstrates how our knowledge of semiconductors has been furthered by optical studies. R. G. Shulman considers trapping and recombination processes arising from nonequilibrium distributions of mobile carriers. J. N. Hobstetter examines the nature and role of structural defects, particularly dislocations, in controlling plastic deformation and other properties of semiconductors.

A. R. Hutson presents a critical survey of the semiconducting properties of some oxides and sulfides, including alkaline earth oxides, sphalerite-wurtzite compounds, and the lead sulfide family. F. J. Morin provides a most illuminating discussion of the electrical, optical, and magnetic properties of oxides of the third transition metals. In the final article on bulk properties, C. G. B. Garrett reviews most competently the subject of organic semiconductors.

The remaining two contributions are concerned with the physics and chemistry of semiconductor surfaces. J. T. Law deals primarily with solid-vapor and solid-vacuum interfaces, while J. F. Dewald treats semiconductor electrodes and hence the semiconductor-electrolyte interface. At the end of the book there is a subject index, but, surprisingly, no author index.

In my opinion this volume is the finest, best organized, and generally most useful collection of survey articles on semiconductors yet assembled. It is easier to gain an over-all picture of the present state of our knowledge of semiconductors by reading this volume than by reading scattered review articles published elsewhere. The individual articles in the present volume are comparable, with respect to quality and method of exposition, to the excellent reviews appearing in the Seitz and Turnbull "Solid State Physics" series.

It is perhaps worth mentioning that the subjects of luminescence and photoconduction, which are closely related to that of semiconduction, might have been treated in an additional chapter or two. As it is, these subjects are not given the comprehensive coverage they deserve. But this is a minor criticism of an otherwise excellent book.

To conclude, this volume is warmly recommended to graduate students and to professional scientists in the several disciplines which constitute the field of semiconductors.

FRANK HERMAN
RCA Laboratories, Princeton, New Jersey

Cumulative Record. B. F. Skinner. Appleton-Century-Crofts, New York, 1959. x + 427 pp. Illus. $6.50.

When B. F. Skinner was scarcely 22 he read a series of articles in which Bertrand Russell examined John B. Watson's behaviorism. Many years later he told Russell that these articles had been responsible for his interest in behavior. "Good Heavens!" exclaimed Lord Russell, "I had always assumed that these articles had demolished behaviorism." Russell may have demolished Watson's theories—not a difficult task; but Watson's spirit is indestructible. Cleaned and purified, it breathes through the writings of B. F. Skinner. Watson rejected philosophic speculation and demanded an objective science of behavior as rigorous as Newton's science of the physical universe; Skinner defends the rejection of speculation with the sharpness of a trained philosopher and presents us with an analysis of behavior that Newton might have envied. Probably no psy-

chologist since James Mill has given us a neater, cleaner, simpler analysis of the human mind.

Among contemporary American psychologists, Skinner has perhaps the greatest appeal to those who like to think of psychology as an exact science. He has five substantial books to his credit, and a great number of articles; all of these demonstrate the importance of the stimulus-response-reinforcement principle. *Cumulative Record* is a reprint of his most important articles, carefully arranged and annotated in such a way as to make the sequence intelligible. Psychologists will be grateful that these papers are now more accessible. Scientists from other fields will find in this volume reassuring evidence that psychology can be made to conform to the Newtonian conception of science.

Some readers may find Skinner's conceptual framework a bit constricting, but none can fail to admire the skill with which he reduces the complexities of behavior to the simplest possible terms, or to envy the serenity with which he looks forward to a world in which the behavior not merely of the rat and the pigeon but also of man can be precisely predicted and expertly controlled. I recommend particularly part 2, "A case history of scientific method," and the two articles in part 3 on the technology of education. *Cumulative Record* is not quite complete enough, however, to give us a full understanding of what psychology can do with human behavior. The reader is urged to glance through Skinner's most recent substantive work, *Verbal Behavior* (Appleton-Century-Crofts, New York, 1957), and then to examine critically N. Chomsky's detailed appreciation of that book *Language* [**35**, 26 (1959)].

ROBERT B. MACLEOD
Department of Psychology, Cornell University

Fundamental Aspects of Reactor Shielding. Herbert Goldstein. Addison-Wesley, Reading, Mass., 1959. xvi + 416 pp. $9.50.

Reactor shielding is a complicated and difficult specialty within the field of nuclear engineering which has received much attention because of its importance for military mobile reactors. The basic mathematical problems of shielding—namely, the computation of the deep penetration of gamma rays and neutrons—are, even in relatively simple cases, much more severe than the problem of computing the criticality of a simple reactor. Reactor theory centers essentially on eigenvalue problems, and there is a single, clearly defined measure of the validity of the theory—how well the computed and the experimental critical masses agree; in shielding theory there is no comparably simple criterion of validity—both the measurement and the calculation of fluxes at large distances are fraught with difficulties and uncertainties.

Because of this basic difficulty, the science of shielding has had to proceed as a blend of semirigorous calculation, experimental intuition, and even, on occasion, black magic. This essential flavor of the shielding art is admirably caught by Goldstein's book. That much of the discussion is not rigorous is surely an accurate reflection of the fundamental nature and difficulty of the shielding problem, as compared, say, with the problem of criticality of reactors.

As the author says in his preface, the book has much of the character of a review rather than of a monograph: for example, in many of the mathematical derivations reference is made to works quoted in the bibliography. The review, however, is a critical one, and the author does not hesitate to point out shortcomings in both shielding experiments and theories.

The book is divided into three major parts: first, a description of the general problem of reactor shielding and of the radiation sources against which shielding is necessary; second, a description of the experimental techniques and devices developed in the United States for carrying out shielding experiments; and third, a review of the mathematical theory of deep penetration of gamma rays and neutrons, together with experimental comparisons.

The writing is fluid and breezy. However, in some cases the cant of the shielding expert is used in a way which may prove confusing to the beginner—for instance, the build-up factor is mentioned on page 15 before it is defined, and the Bragg-Gray principle is invoked without a full explanation. Since many of the real problems of shielding are associated with mobile—that is military—reactors, much of the development described by Goldstein was classified information at the time it originated. As a result, references must sometimes be made to literature which is still classified, a certain source of annoyance to those readers who do not have access to the classified literature.

Although it is written from the point of view of reactor shielding, Goldstein's book will be useful, and can be recommended, to all who have to deal with radiation shielding—whether of isotopes, medium-energy accelerators, or reactors. As befits a review-type book, the bibliography is superb, even though confined largely to the American literature.

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Women and Work in America. Robert W. Smuts. Columbia University Press, New York, 1959. x + 180 pp. $4.50.

In this small, easy-to-read book the author contrasts women's work (chapter 1) and working women (chapter 2)—their conditions of work (chapter 3), their attitudes, and the attitudes of others toward them (chapter 4)—at the turn of the century with current mid-century practices and attitudes in the United States. He quotes extensively from contemporary sources, as he did in his earlier monograph, *European Impressions of the American Worker*—also a product of his research for Columbia University's Conservation of Human Resources Project.

Drawing heavily on Census statistics, too, the author sketches today's women workers as essentially well off by comparison with their earlier counterparts. He finds more striking than changes in their occupations in the labor market "the shift of wives and mothers from household activities to the world of paid employment." But, he observes, "Today, as always, most of the time and effort of American wives is devoted to their responsibilities within the home and family circle." He concludes that "once her children are in school, the modern mother has more freedom of choice than the single woman had in 1890." Working conditions, he reports, are better for most women workers, but barriers to training and advancement still exist, along with disagreement about legislation aimed at their removal. In the modern separation of home and work Smuts sees the origin of the dilemma of the woman of today who wants to achieve success in her work without neglecting family responsibilities. He notes that our modern economy creates a similar problem for men. Examining the "causes

rather than the momentous consequences of changes in women's work," he offers no predictions except that the increasing employment of wives and mothers will "leave a deep imprint on every side of American life during the second half of the century."

The flaws in this interesting, documented, quotable book affect the research worker more than the casual reader. Among such flaws are Smuts' failure to mention inflation as a cause of employment of women, especially of older women and widows; his failure to cite such basic discussions of his subject as Hazel Kyrk's, in *The Family in the American Economy*; and a style of citing sources that is onerous to a reader interested in dates of publication.

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Celestial Mechanics. E. Finlay-Freundlich. Pergamon Press, New York, 1958. viii + 150 pp. $7.50.

In a small volume on a subject as vast as celestial mechanics it is impossible to give more than a general introduction and an exposition of a few selected topics.

The introductory material consists of an elementary treatment of the two-body problem and a chapter on the n-body problem, with emphasis on Lagrange's stationary solutions. This chapter concludes with a discussion of Hill's curves of zero velocity in the restricted problem of three bodies and the periodic solutions in the vicinity of the stationary solutions.

One of the topics that the author selected for more detailed treatment is contained in the chapter entitled "Application of the theory of Hamilton-Jacobi to the three-body problem." The theory of canonical transformations is presented briefly but adequately. The integration of the two-body problem by Jacobi's method is then given as preparation for applications to perturbational problems, an outline of which is presented in the next chapter.

Two more topics are treated in considerable detail: "the two-body problem for extended deformable bodies" and "the motion of the apsidal line in relativistic mechanics."

The book will serve as a useful introduction to the subject for students with adequate mathematical preparation. The serious student will find his appetite whetted for more, especially for more concerning applications of the Hamilton-Jacobi theory to the problem of perturbations. The bibliographies given in the various chapters will direct him to some of the standard works, but these are not detailed enough to offer specific help.

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Landscape from the Air. A physical geography in oblique air photographs. F. J. Monkhouse. Cambridge University Press, New York, 1959. ix + 53 pp. Illus. Paper, $1.75.

Air photography has brought a new tool to the classroom. Geographers, geologists, foresters, pedologists, engineers, planners, military leaders, and others all make extensive use of air photographs—pictorial likenesses mechanically achieved. About 45 percent of the earth's land area has been photographed from the air; coverage of the United States is virtually complete.

Landscape from the Air was written primarily for geographers and geologists, for use in conjunction with topographic maps to envisage types of landscape that one might never be able to visit in person. Fifty-two oblique aerial photographs —most of them of Europe but some of North America, Africa, and Asia—are used to depict landscapes, under the following headings: "Rock types"; "Structure"; "Vulcanicity"; "Earth sculpture"; "Underground drainage"; "Rivers and river valleys"; "Glaciation"; "Desert lands"; "Coast lines"; and "Lakes and lake-basins." The photographs used were carefully and meticulously selected from among thousands.

Beneath each photograph are given the names of major features and the short numbers of the relevant topographic maps. Moreover, in the majority of instances the exact orientation of the photograph is given. Then follows a brief description of the main features to be seen in the photograph. Every effort has been made to make the text self-explanatory, but to get the most from a given illustration the "photo-interpreter" should have some background knowledge of geography and geology, for only then will he know what to look for. Proper interpretation of aerial photographs is positively dependent on professional competence.

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New Books

Analysis of Linear Systems. David K. Cheng. Addison-Wesley, Reading, Mass., 1959. 439 pp. $8.50.

Astronomy. Theodore G. Mehlin. Wiley, New York; Chapman & Hall, London, 1959. 400 pp. $7.95.

The Economics of Freedom. American capitalism today. Massimo Salvadori. Doubleday, Garden City, N.Y., 1959. 264 pp. $4.50.

Free Radicals. An introduction. A. F. Trotman-Dickenson. Methuen, London, Wiley, New York, 1959. 148 pp. $2.50.

Geochemical Methods of Prospecting and Exploration for Petroleum and Natural Gas. A. A. Kartsev, Z. A. Tabasaranskii, M. I. Subbota, G. A. Mibilevskii. English translation edited by Paul A. Witherspoon and William D. Romey. Univ. of California Press, Berkeley, 1959. 372 pp. $12.50.

Handbook of Diet Therapy. Dorothea Turner. Univ. of Chicago Press, Chicago, Ill., ed. 3, 1959. 237 pp. $5.

The Harvey Lectures. Delivered under the auspices of the Harvey Society of New York, 1957–1958. Series 53. Academic Press, New York, 1959. 269 pp. $7.50. Contents: "An epidemiological study of illness in families," J. H. Dingle; "Myxomatosis in Australian wild rabbits—evolutionary changes in an infectious disease," F. Fenner; "Structure and infectivity of tobacco mosaic virus," H. Fraenkel-Conrat; "Bacterial reproduction," J. Lederberg; "Enzymatic synthesis of deoxyribonucleic acid," A. Kornberg; "Some reactions of lymphoid tissues to stimulation by antigens," A. H. Coons; "Cell division," D. Mazia; "Correlation of roentgenological and pathological changes in some diseases of the lung," J. Gough; "Extracorporeal maintenance of cardiorespiratory functions," J. H. Gibbon, Jr.

The Invertebrates. Smaller coelomate groups: Chaetognatha, hemichordata, pogonophora, phoronida, ectoprocta, brachipoda, sipunculida, the coelomate bilateria. vol. 5. Libbie Henrietta Human. McGraw-Hill, New York, 1959. 791 pp. $13.50.

Linear Network Analysis. Sundaram Seshu and Norman Balabanian. Wiley, New York; Chapman & Hall, London, 1959. 585 pp. $11.75.

The Many Body Problems. Summer school course in theoretical physics given at the University of Grenoble, 1958. Wiley, New York; Methuen, London; Dunod, Paris, 1959. 675 pp. $15.

Medical Museum Technology. J. J. Edwards and M. J. Edwards. Oxford Univ. Press, New York, 1959. 182 pp. $3.40.

Organic Chemistry. Melvin J. Astle school course in theoretical physics given 1959. 781 pp. $7.50.

Package Design Engineering. Kenneth Brown. Wiley, New York; Chapman & Hall, London, 1959. 276 pp. $8.50.

Physiology of Insect Development. Frank L. Campbell, Ed. Univ. of Chicago Press, Chicago, Ill., 1959. 181 pp. $4.

Plane Trigonometry. A. W. Goodman. Wiley, New York; Chapman & Hall, London, 1959. 284 pp. $4.50.

Reports

Lactation Hair in the Asiatic Squirrel and Relationship of Lactation Hair to Mammary Hair

Abstract. A hair growth around the nipples during lactation is described in two species of the Asiatic squirrel genus *Callosciurus*. The term *lactation hair* is coined for this phenomenon, which is shown to be different from *mammary hair* in the sense for which that term was coined.

Pfeiffer (*1*) described the hormonal control of the changes in the color of the patch of hair around the mammary gland during lactation in the mountain beaver (*Aplodontia rufa*). The normal belly fur around the nipple, in this animal, falls out and is replaced during lactation by coarser black hair.

The only similar phenomenon in mammals that had been noted up to then was the appearance of two patches of cinnamon-colored hair on the thorax in *Erethizon* (*2*). These patches are, however, associated with estrus and not lactation.

Recently, while surveying the mammary glands of rodents in the mammal collection of the United States National Museum, I came across two more examples of special mammary-gland hair development during lactation in Asiatic squirrels.

Apparently, in *Callosciurus leucomus* as the nipple and mammary gland enlarge prior to lactation, the normal belly fur around the teats is replaced by a cottony white hair. This white hair in turn is lost, leaving a bare area around the fully developed lactating nipple.

The sequence may be seen in the following skins in the National Museum collection: 216791—spots of white fur around nipples; 216784—area around nipples becoming bare, some white hairs still present; 216785—nipples almost bare, a few white hairs around the hindmost nipple on the left side; 216773 and 216788—area around nipples completely bare.

In *Callosciurus hippurus* lactation is accompanied by the acquisition of a sparse growth of coarse hairs around the nipples. The ordinary belly fur does not fall out; these "lactation hairs" (as I propose to call them) are added to it. The effect is of a dark spot around the nipple, so that one's first impression is that the fur is milk-stained.

Examination under a dissecting microscope shows these lactation hairs to be long and coarse. They are alternately banded with black and rufous red, the pattern reminding one of the guard hairs of the back (which are banded with black and buff). The hairs are flattened and tend to curl into loose spirals exactly like human pubic hair, which this lactation hair strongly resembles. I have never seen hair like this in any other rodent.

These hairs may be seen on museum skins, 38252, 29059, and 84443. The last has the largest nipples of the three and the best developed lactation hairs. In it, the dark spots around the nipples merge to form two continuous bands along the belly.

Pfeiffer believed that these patches of altered hair around lactating nipples were mammary hairs in the sense that the term is used by Bresslau (*3*)—that is, hairs from whose follicles the mammary glands originated. Examination of the pertinent literature convinces me that Pfeiffer's homology is incorrect.

In monotremes, mammary glands originate from the follicles of precociously developed mammary hairs that form in two broad bands along the belly of the embryo. Nipples do not develop (*4*), but eventually the mammary glands (still opening into the follicles of the mammary hairs) come to be concentrated into two relatively restricted gland areas.

In marsupials, the mammary glands arise from invaginations or inward proliferations of the epidermis that are later converted into nipples. From the bottoms of these primordia, hair follicles originate, and from the hair follicles, mammary and sebaceous glands. The hair follicles eventually degenerate, leaving mammary glands and sebaceous glands opening into the bottom of the nipple primordia (*5*). These transient hairs are presumably homologous to the mammary hairs of monotremes.

In placental mammals the process is similar, except that the nipple primordia develop from a continuous ridge, and mammary glands are less conspicuously associated with mammary hairs, although they have been reported, for example in horses (*6*), pigs (*7*), and man (*8*).

If these mammary hairs were to persist into adulthood, they should be found on the tips of the nipples protruding from the openings of the mammary glands. In many squirrels they do persist (as ventral vibrissae) and are found in precisely that position, although upon subsidiary nipple primordia that have separated and migrated from the nipples proper (*9*).

The lactation hairs of *Aplodontia* and *Callosciurus* occur in broad patches around the nipple, a position that does not suggest that they are associated with the developing mammary gland.

In addition, lactation hairs are far too numerous to be mammary hairs. The number of mammary hairs associated with each nipple is always small; the numbers given for *Trichosurus* are 13, for *Parameles*, 9 (*5*), and for *Homo*, 8 (*8*).

Of course, it is possible that the original mammary hair follicles migrated peripherally and broke up into numerous follicles to form lactation hairs. There is no evidence for this, however, and it seems to me more likely that lactation hairs develop in place from normal hair primordia, at the time of lactation.

Lactation hairs, therefore, could not be a "physiological relict," as Pfeiffer suggested, but are probably a specialization whose function is obscure. They should not be confused with mammary hairs; this term should be reserved for hair follicles associated with the earliest development of mammary glands.

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2 March 1959

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* **125**, 16 (1957)].

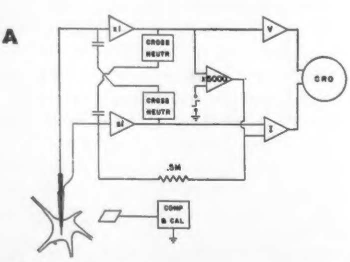
Voltage Clamp of Motoneuron Soma

Abstract. Concentric microelectrodes were used to voltage-clamp spinal motoneurons. With depolarizing voltage steps, current transients often appear, with some latency and in all-or-none fashion. Voltage-current relations indicate a two- to threefold reduction in resistance between inside and outside when the cell fires. These results suggest that activity does not involve the whole soma-dendritic membrane.

Spikes recorded from spinal motoneurons with intracellular electrodes present two components which have been called A and B (*1*). It has been suggested (*1–3*) that the first component results from activity of the initial segment of the axon, and the second component, from activity of the soma (and perhaps of the dendrites). Alternatively (*4*), the first component has been ascribed to activity of the soma, and the second, to activity of the dendrites. More recently, evidence has been produced suggesting that the cell soma is not fully invaded by activity even during the second component (B) of the spike (*5, 6*). Voltage-clamp techniques have been applied to the study of motoneuron firing in the hope that some features of their impulse production could be clarified by the results obtained with this method.

Concentric microelectrodes, similar to those previously used by Tomita (*7*), were employed for impaling motoneurons. The smaller microelectrode was used to record the potential difference between cytoplasm and indifferent electrode while the currents required to clamp at any desired voltage were passed through the larger microelectrode. Both microelectrodes were connected to a unity-gain "negative capacitance" cathode follower (*8*), and circuits were available for neutralizing the capacity between the two microelectrodes. The feedback amplifier used to deliver currents through the external microelectrode had a gain of 5000 for direct current, and the current was measured as the potential drop occurring across a 0.5-megohm resistor. Measurement of the resistance of each electrode, and of the fraction of these resistances which was common to both electrodes, was made possible by accessory circuits not shown in the block diagram of Fig. 1*A*. The potential records led off by the internal microelectrode (Fig. 1*C*) revealed the degree of clamp of the region surrounding the electrode tip, but it should be noted that these records can give no indication of the spatial extent of the voltage clamp.

Tasaki and Spyropoulos (*9*) have found that the squid giant axon behaves in a nonuniform manner under the voltage-clamp conditions which they employed. With depolarizing voltages near threshold, some parts of the membrane became fully active while other parts remained at rest. If this same phenomenon occurred in motoneurons, interpretation of the results would become ambiguous. However, nonuniformity has not been demonstrated in motoneurons, and it appears reasonable, as a first approach, to consider that the cell soma is isopotential, as has already been assumed by previous workers (*1, 3, 5, 10*) on theoretical grounds. The results of our experiments will be examined in light of this assumption, but the assumption may have to be abandoned if contrary evidence is found.



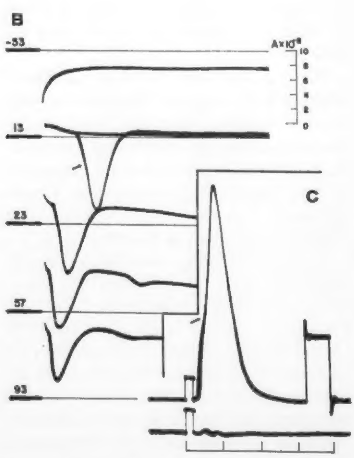


Fig. 1. (*A*) Block diagram of experimental arrangement. (*x*1) Unity-gain, negative-capacitance cathode followers; (Cross neutr.) capacity neutralization circuits; (*x*5000) clamping amplifier; (*V* and *I*) direct-coupled amplifiers measuring potential of internal microelectrode and current through external microelectrode, respectively. "Comp" compensates for contact and tip potentials, and "Cal" provides calibrating pulses between preparation and ground. The gain of the *x*5000 amplifier must be reduced at higher frequencies to prevent oscillation. (*B*) Currents through external microelectrode during clamp at different voltages. Clamping voltages are indicated (in millivolts) by numbers at left. At 57 and 93 mv there is evidence of repetitive firing. (*C*) Potentials recorded by internal microelectrode following antidromic stimulation. The upper record was made in the absence of clamp; the lower record was made during voltage clamp. The square wave is a 20-mv calibration. Arrows indicate A-B inflection; 1-msec time marks apply to records B and C.

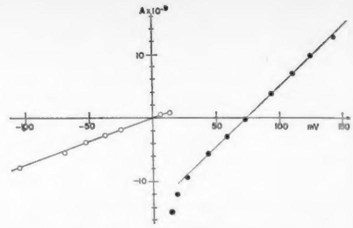


Fig. 2. Plot of data from experiment illustrated in Fig. 1*B*. (Abscissa) Potential recorded from inner pipette during clamping pulse measured from resting value; (ordinate) intensity of current through external microelectrode. Outward current is positive.

Typical results obtained with this method are illustrated in Fig. 1*B*. Hyperpolarizing voltage steps produce inward currents which start at high value and decay as shown in the top record. With weak depolarization (not illustrated), the current is the mirror image of that produced by weak hyperpolarizing voltages, but with stronger depolarization (13 mv in Fig. 1*B*) there is a delayed transient reversal of the current, which follows a course similar to that of a conventional spike. As the depolarization is increased (23 to 93 mv in Fig. 1*B*), the transient inward current becomes less delayed and decreases in amplitude until finally the current is always outward-directed.

Latency of the transient inward current can be explained if it is assumed that the low threshold A area is separated from the clamped area by a series resistance through which the membrane capacity must be charged. Since the depolarization required for firing the B area (arrow in Fig. 1*C*) is much higher than threshold for the A area (*1, 11*), the B area must be at least partly unclamped because a B current transient frequently occurs as a consequence of A activity when the clamp is just threshold for A (13 mv, Fig. 1*B*).

Figure 2 is a plot of the data illustrated in Fig. 1*B*. The open circles in this figure measure the final values of the currents required to clamp the potential of the cytoplasm at different hyperpolarizing or weak depolarizing values. The slope of the line through these points measures conductance between cytoplasm and outside fluids at rest, and the values obtained are in agreement with those determined by different methods

(3, 12, 13). The solid circles measure the values of the current at the peak of the transient phase evoked by depolarization. The line through them intercepts the abscissa at 70 mv, a value similar to the height of the spike recorded in the absence of clamp (Fig. 1C). It can be argued that the slope of the line through the solid circles should give an approximate value of the conductance between cytoplasm and external fluids at the peak of activity. If this is correct, the results indicate that the resistance measured between inside and outside with the method described decreases by a factor of only 2 to 3 during activity. Two principal sources of error should be considered: On the one hand, capacity of the unclamped regions of the motoneuron tends to decrease the value of the resistance measured during activity, since this measurement is made a short time after application of the clamping pulse; on the other hand, any resistance (other than membrane resistance) common to both electrodes will not only decrease the effectiveness of the clamp on the membrane but will also decrease the percentage change in measured resistance between rest and activity by adding a constant quantity to each.

When the clamped region separates one part of the neuron from another, voltage changes in one part cannot affect the other. Thus, the clamped area cannot lie between A and B regions, since A activity elicits B firing even in the presence of the clamp. The foregoing results are consistent with the original hypothesis (1–3) that the A spike originates in the axon but suggest that the B spike does not involve more than a part of the soma-dendritic membrane.

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18 February 1959

Cortical Correlates of Auditory Localization

Abstract. Responses were recorded simultaneously from a number of electrodes on the auditory cortex of one hemisphere of cats. Response amplitudes at different electrodes reached maxima and minima at different real or apparent locations of a click stimulus.

Although we have fairly extensive knowledge of the stimulus correlates of auditory localization, the physiological correlates still appear to be undetermined. The experimental evidence presently available indicates two major possibilities. One is that spatial location of the auditory stimulus is translated into locus of maximal activity within one side of the auditory system. This type of theory, generally referred to as a place theory, has been seen often, not only in audition (1) but in the "local sign" theories of other sensory modalities as well. The other possibility is that auditory localization is related to the ratio of the response magnitudes of the two sides of the auditory system (2). This may be referred to as a bilateral ratio theory. The research reported here was designed to test the validity of a place principle in auditory localization.

A six-channel electroencephalograph was used in conjunction with a bank of six oscilloscopes to photograph and measure simultaneous responses to click stimuli at six locations on the auditory cortex (AI and AII) of one hemisphere. Changes in the magnitudes of the responses recorded from each of the electrode locations were explored as a function of changes in the real and apparent location of the click stimuli (3). The subjects were 15 cats anesthetized with Nembutal.

Moving an actual (click) source in space gives the type of results illustrated in Fig. 1, which shows response amplitudes at different electrode locations reaching maxima or minima, or both, at different source locations. These data suggest (i) that there may be in the auditory cortex of one hemisphere elements that are differentially sensitive to the spatial location of a stimulus source (4) and (ii) that these elements are not distributed homogeneously through the auditory area.

When apparent location of the click stimuli is manipulated by changing the binaural time interval while holding the binaural intensity ratio constant, results of the type illustrated in Fig. 2A are obtained. These data were obtained with click stimuli of equal loudness in both ears. It can be seen that response amplitudes at different electrode locations reach peaks or troughs at different binaural time intervals (or apparent locations). When the loudness of the first click is made greater than the loudness of the second click, the relationship among average or general response magnitudes at the various electrodes changes, as is illustrated by comparing Figs. 2A and 2B. In Fig. 2A electrodes 2, 3, 4, and 5 show similar average response magnitudes, while in Fig. 2B the response magnitudes are clearly different, the average response magnitude at electrode 2 being enhanced, that at electrode 4 being relatively unaffected, and those at electrodes 3 and 5 being depressed. The curves in Fig. 2B also are more nearly parallel than those in Fig. 2A. The extent to which these changes take place as the result of manipulation of the binaural intensity ratio is related, as might be expected, to the amount by

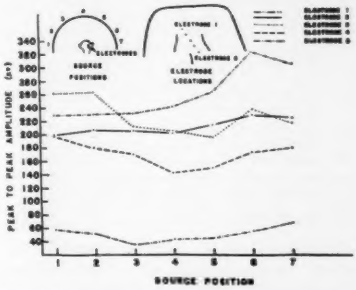

Fig. 1. Amplitude of cortical response to clicks (28 db SL at electrode 1) as a function of source position and electrode location.

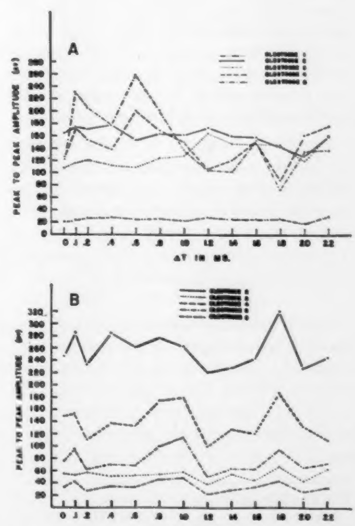

Fig. 2. Amplitude of cortical response to binaural click stimuli as a function of binaural time delay (Δt). First click, ipsilateral. *A*, First click, 20 db SL; second click, 20 db SL. *B*, First click, 30 db SL; second click, 10 db SL.

which the intensity ratio is changed. These graphs were obtained from the same animal and with the same electrode locations, except as noted in the legends. Similar results have been obtained with several orientations of the electrode array within auditory area AI, and with click No. 1 both ipsilateral and contralateral to the recording electrodes.

These data suggest that the angular location of auditory stimuli may be represented in the auditory cortex of one hemisphere by means of a place principle.

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9 February 1959

Nature of Colchicine Resistance in Golden Hamster

Abstract. The unresponsiveness of the golden hamster to colchicine has been shown to be the result of a resistance of individual cells to the drug. This resistance makes it possible to use hamsters with heterotransplanted tumors for testing the in vivo effects of colchicine on the tumors, with no toxic host reactions.

Orsini and Pansky (*1*) have reported a resistance on the part of the golden hamster to the toxic and mitotic inhibitory effects of colchicine. In a study of lethal effects, Turbyfill and Soderwall (*2*) showed that this resistance was at least 100 times greater in the hamster than in other animals. Whether this unresponsiveness is the result of a systemic inactivation of the drug or the result of a resistance of the individual cells has not been determined. The experiments described in this report indicate that the golden hamster has a true cellular resistance to the action of colchicine.

The first experiment was undertaken to determine whether heterologous tissues grown in hamsters were sensitive to colchicine. Three transplanted human testicular tumors (*3*), a teratocarcinoma of the ovary of a mouse (*4*), and a spontaneous anaplastic hamster carcinoma (*5*) were maintained in the cheek pouches of cortisone-conditioned weanling golden hamsters, as described previously (*3, 6*). Experimental animals bearing tumors of approximately the same size received intraperitoneal colchicine (*6*) in dosages listed in Table 1, while tumor-bearing controls received no treatment. The tumors and a piece of duodenum were removed 18 hours later and examined microscopically. By means of an ocular reticule, the mitoses in 40 areas of constant size were counted in each tumor. Likewise, the mitoses were counted in 40 of the host's intestinal crypts, which were considered to be similar to each other in size and shape.

In a second experiment to determine the effect of colchicine upon isolated cells in vitro, we grew embryonic hamster tissue in plasma clot and human cells of the D-189 strain (Mavar) (*7*) on glass. The growth medium was made up of calf serum, chick embryo extract, and Hanks balanced salt solution (20:10:70), to which Eagle's basal medium concentrates, penicillin, and streptomycin were added. When suitable growth was obtained, 0.2 ml of serially diluted colchicine in balanced salt solution was added to the cultures (the final concentrations are listed in Table 2). Control cultures received only balanced salt solution. Six hours later they were fixed in Bouin's fluid and stained. At least 200 consecutive human and 400 hamster mitoses were differentially counted for each concentration of colchicine. The results were expressed as the percentage of mitoses which had ball-like configurations with no evident spindles typical of colchicine-induced metaphase arrests.

Table 2. Effects of colchicine upon human and hamster cells in vitro. Values represent the percentage of mitoses with the configuration of colchicine-induced "arrests" (see text).

Final concentration	Human strain D-189 (Mavar) cells	Hamster embryonic cells
(Control)	6	7
$10^{-9}M$ colchicine	16	
$10^{-8}M$ colchicine	36	
$10^{-7}M$ colchicine	99	5
$10^{-6}M$ colchicine	100	36
$10^{-5}M$ colchicine		85
$10^{-4}M$ colchicine		95
$10^{-3}M$ colchicine		96

The results of mitotic counts for the in vivo experiments listed in Table 1 indicate that colchicine had no effect on the mitotic index (the number of mitoses in a given area) of the hamster intestinal crypts or of the spontaneous hamster carcinoma within the dosage range used. There was a striking increase, however, in the mitotic index of heterotransplanted tissues of human and mouse origin, especially at the higher dosages employed. These effects generally began to appear at the 0.1 mg per 100 gram body-weight level but occasionally were noticed at the 0.05 mg per 100 gram level. Cells arrested in vivo displayed mitoses typical of colchicine treatment (*8*).

No abnormalities attributable to colchicine could be detected on gross examination in the 65 hamsters treated at 0.25- and 1.0-mg/100 g levels. This was in contrast to findings for a group of 21 C_3H mice treated with the same doses of colchicine on a weight-for-weight basis. After 18 hours four mice died and the remainder had humped backs, ruffled fur, and marked diarrhea.

The results of in vitro studies (Table 2) indicated that hamster cells had at least a 100-fold greater resistance to colchicine than human cells. A few normal metaphases viewed on end were indistinguishable from colchicine-induced metaphases, and this accounted for the "arrests" noted in the control group. Many normal anaphases and telophases could be found in the hamster tissues at concentrations of colchicine as great as $10^{-5}M$, indicating that in spite of the large percentage of arrests found, considerable resistance was maintained at this high level.

Table 1. Effects of colchicine on heterologous and homologous tissues grafted in the hamster. All values represent the average number of mitoses per unit area per animal studied (see text), plus or minus one standard deviation. Number of animals in parentheses.

Tissue	No. of mitoses: Control	Dosage*: 0.05 mg	0.1 mg	0.25 mg	1.0 mg
Pitt 89 (human) choriocarcinoma)	46 ± 12 (11)	112 ± 97 (8)	569 ± 154 (7)	540 ± 79 (5)	540 (2)
Pitt 61 (human embryonal carcinoma)	45 ± 8 (6)		104 ± 16 (4)	493 ± 42 (4)	
Deac 3 (human embryonal carcinoma)	63 ± 29 (16)	64 ± 12 (5)	175 ± 81 (6)	574 ± 42 (7)	
Mouse ovarian teratoma	64 ± 12 (6)		262 ± 183 (5)	744 ± 89 (4)	
Hamster carcinoma	13 ± 4 (8)			14 ± 2 (10)	14 ± 7 (9)
Hamster intestinal crypts	62 ± 15 (16)	69 ± 14 (10)	63 ± 12 (19)	57 ± 12 (17)	64 ± 10 (7)

* Doses are of colchicine (1 mg/2 cm^3) per 100 g of body weight.

This study of human, mouse, and hamster tissues, both in vivo and in vitro, demonstrated that normal adult, neoplastic, and embryonic hamster tissues have a cellular type of resistance to colchicine that is at least 100 times greater than that of human cells. This degree of resistance for hamster cells in vitro was similar to that previously reported in in vivo toxicity experiments in which the hamster was compared with other mammals (2).

The existence of a cellular resistance to colchicine in the hamster will make possible investigation of the effects of high and long-continued doses of colchicine on heterotransplanted tissues, embryonic or neoplastic, with no toxic host reactions. This resistance is an example of a genetically transmitted tolerance, and, if gene-controlled, could be used as a marker in transformation studies upon mammalian cells in vitro (9).

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24 February 1959

Adsorption of Antibody in vitro and Magnitude of the Schultz-Dale Reaction of Guinea-Pig Ileum

Abstract. Studies show that the adsorption of rabbit antiovalbumin-I^{131} on guinea-pig ileum conforms to a Langmuirian isotherm, and that the physiological response to challenge with antigen depends upon the amount of antibody bound to the tissue.

Recently, Germuth and McKinnon (1) showed that antigen-antibody complexes, formed in antigen excess, would produce gross anaphylaxis of varying degrees of severity in the normal guinea pig, and Trapani, Garvey, and Campbell (2) demonstrated a quantitative relationship between the antigen-antibody ratio of the complex and the degree of the Schultz-Dale response.

This report concerns the quantitative relationship between the antibody content of the tissue and the magnitude of the specific response. Since active immunization, or even passive transfer of antibodies, could not be expected to provide a reproducible degree of immunological sensitivity, a method of sensitizing tissues in vitro was investigated (3). Although sensitization of isolated tissues by exposure to crude antisera has been reported (4) we do not know of any studies in which an attempt was made to detect whether antibody was actually adsorbed on the tissue, or of data giving a quantitative relationship between the concentration of antibody bound to the tissue and the magnitude of the Schultz-Dale response.

The present report (5) shows that the I^{131}-labeled gamma-globulin fraction of rabbit antiovalbumin can be adsorbed by guinea-pig ileum in proportion to the protein concentration in the *bulk phase* and that the response of the muscle to antigen is a function of the amount of antibody remaining on the tissue.

The antigen used in these studies was four-times-crystallized ovalbumin prepared by the method of Keckwick and Cannan (6). The antiserum was prepared by injecting rabbits with ovalbumin for 6 weeks, in accordance with an injection schedule not yet published (7). Animals were bled by cardiac puncture, the serum was separated, and the gamma globulin was prepared by reprecipitating the antiserum four times in the presence of ⅓-saturated ammonium sulfate. The preparation was dialyzed against repeatedly changed 1-percent NaCl and dried from the frozen state. The antibody content of the soluble protein was 32.5 percent, as determined by the quantitative precipitin technique; hence, it is likely that the preparation contained other antibodies as well as normal globulins. Antiovalbumin-I^{131} was prepared from a portion of this material by the method of Hughes and Straessle (8). The material employed in the studies discussed in section 1, below, contained 0.01 mole of iodine per mole of gamma globulin and had a specific activity of 0.35 μc/mg gamma globulin.

1) To determine the effect of I^{131} gamma globulin concentration and washing upon the residual radioactivity of the tissue, ileal strips measuring 2.5 cm in length when relaxed were prepared from intestines of normal male guinea pigs (350–400 g) according to the method of Feigen and Campbell (9). These were immersed in muscle baths, constructed from sintered glass filters, having a capacity of 30 ml, each

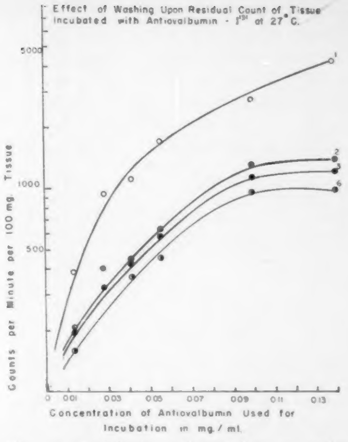

Fig. 1. Residual radioactivity on strips of normal-guinea-pig ileum incubated in various concentrations of an I^{131}-labeled gamma-globulin fraction of rabbit antiovalbumin. Curves 1, 2, 3, and 6 represent residual radioactivity after the first, second, third, and sixth washings.

containing a different concentration of I^{131}-labeled gamma globulin, ranging from 0.014 to 0.140 mg/ml. All tissues were incubated in 30 ml of Tyrode solution for 60 minutes at 27°C and then washed with 30-ml portions of fresh Tyrode solution at 27°C. The radioactivity was measured in a well-type crystal (NaI) scintillation counter. The counting efficiency with an I^{131} standard was 33.3 percent. The tissue was mounted on a glass rod and was immersed in a tube contained in the well of the scintillation counter. The radioactivity of the system was measured in the presence and in the absence of tissue, and the residual radioactivity on the tissue was obtained from the difference in the measurements. The washing and counting operations were carried out for six complete washing cycles. The results, presented in Fig. 1, are mean values for two strips tested at each concentration.

Since, as is shown in Fig. 1, the residual radioactivity of a tissue appears to bear a constant relationship to the concentration of I^{131}-labeled gamma globulin used in the original incubation, and since the radioactivity is not greatly reduced between the second and sixth washings, it appeared possible to test the data of curve 3 for conformance to the Langmuir adsorption isotherm. A convenient form of Langmuir's equation is

$$C/a = (1/\alpha\beta) + (C/\beta) \qquad (1)$$

in which C is the concentration of antiovalbumin in milligrams per milliliter, a is the amount (in milligrams) of adsorbate taken up by 100 mg of tissue, and α and β are constants. Accord-

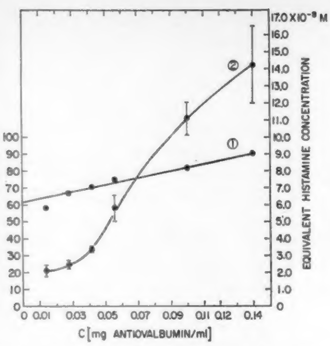

Fig. 2. Curve 1 (left ordinate) is a plot of C/a against C in which C is the concentration of antiovalbumin in the bulk phase and a is the amount (in milligrams) of antiovalbumin remaining per 100 mg of tissue after the third washing. Curve 2 (right ordinate) is a plot of the physiological response to 2 mg of antigen of tissues that had been incubated for 1 hour in antiovalbumin and washed three times before testing. The equivalent histamine concentration, a measure of the physiological response, is obtained graphically from histamine standardization curves carried out for each muscle strip. The vertical bars indicate standard errors of the respective means.

ing to this relationship, a plot of C/a against C should give a straight line having a slope of $1/\beta$ and an intercept of $1/\alpha\beta$. Curve 1 of Fig. 2 shows that the data, in the range between 0.028 and 0.140 mg of I^{131}-labeled gamma globulin per milliliter are adequately described by a line with a slope of 206.7 and an intercept of 61.5, from which the values of β and α are found to be 0.0483 and 3.35, respectively.

2) To determine the dependence of Schultz-Dale response on concentration of antibody used for incubation, tissues were incubated at 27°C for 60 minutes in nonradioactive antiovalbumin gamma globulin, the same range of concentrations being employed as in part 1. These tissues were washed three times at 27°C and then equilibrated at 37°C for 30 minutes before they were challenged with antigen in the Schultz-Dale test. Frontal writing levers were used to obtain kymographic records of muscular response. Each muscle was titrated with at least three doses of histamine before and after challenge with 2 mg of ovalbumin, the second histamine titration being carried out in a dosage range which was closely equivalent to the muscular response to antigen. The histamine equivalent of the specific contraction was obtained by interpolation from the histamine calibration curve of the particular strip of gut.

Curve 2 of Fig. 2 illustrates the dose-response characteristics of challenged muscle strips that had been incubated in the same concentrations of the antiovalbumin preparation that had been used in the experiments with the radioiodinated gamma globulin. Each point is the average of 11 to 17 values, the modal number being 16. As can be seen from the magnitudes of the standard errors, the evaluation of response at the higher protein concentrations is subject to a great deal of error because the sigmoidal dose-response curve with respect to histamine tends to flatten out at higher doses, making interpolation uncertain at near-maximal responses to antigen; for this reason incubation experiments were not made in the range beyond 0.14 mg of antiovalbumin per milliliter. Muscles could not be sensitized in concentrations of antibody lower than 0.014 mg of antiovalbumin per milliliter at 27°C.

Taking 0.014 mg/ml as the limiting value for sensitization, we can, on the basis of certain assumptions, make an approximate calculation of the amount of antibody necessary to set off a minimal reaction. Since preliminary experiments showed that there is no difference in the binding properties of normal and immune radioiodinated gamma globulin, we can assume that the binding of antibody is not preferential—hence, that the amount bound will be determined by the proportion of antibody in the total protein preparation, in this case 32.5 percent. The amount of total protein taken up by 100 mg of tissue from a concentration of 0.014 mg/ml is found to be 2.4×10^{-4} mg; from this finding, a value of 7.8×10^{-5} mg of antibody per 100 mg of tissue is obtained as the minimal ratio for discharge of the Schultz-Dale reaction.

The studies discussed in this report have shown that rabbit antiovalbumin can be bound to the serosal surface of guinea-pig ileum in proportion to the concentration of the antiovalbumin in the bulk phase. Since the relationship conforms to a Langmuirian isotherm, we can infer that these molecules form a monolayer; this does not imply that the combining sites are limited to the cell surfaces or to the superficial layer of cells. The reaction to antigen is also dependent on the amount of antibody bound; whether or not this reaction involves the formation of toxic complexes cannot be determined from the experiments discussed here.

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19 January 1959

Variations in Style Number and Other Gynoecial Structures of Lychnis alba

Abstract. Consistent variations in style number (from the typical five), ranging from zero to ten, inclusive, are found in ovaries of *Lychnis alba* flowers. The number of carpels, placentae, and vascular strands of a given ovary usually varied directly with the number of its styles.

Ovaries of the pistillate flowers of *Lychnis alba* Mill. typically bear five styles. However, some descriptions read: "Styles 5 rarely 4" (*1*); "Styles 5 occasionally 4 or rarely 3" (*2*); "Styli 5, rarius 4, v. hinc inde 3" (*3*). Westergaard (*4*), Warmke and Blakeslee (*5*), and Warmke (*6*) published illustrations of artificially induced polyploid hermaphrodite and other flowers of *Melandrium* (*Lychnis*) with ovaries bearing differing numbers of styles but did not comment upon them.

Earlier I had found ovaries of *Lychnis alba* with two, three, four, six, and seven styles. These variations appeared so frequently and consistently that I initiated a statistical survey in 1958 to determine what variations in the number of styles actually occurred in the species. The preliminary results are described in this report.

Flowers were collected from plants (i) in a greenhouse; (ii) near Iowa City and West Liberty, Iowa; and (iii) near Bemidji, Minn. Thirty daily collections were made during May and June 1958 from greenhouse plants (*7*); 29 spaced, individual collections were made outdoors in Iowa, and 31 were made in Minnesota. All pistillate flowers were taken from every plant in every plot studied. Collections were total, and there were no special selections from any plant or plot suspected of producing, or known to produce, ovaries with differing numbers of styles. Collections in Minnesota clover-alfalfa fields covering several

acres were made from smaller subplots selected at random, or were made by collecting all *Lychnis* flowers encountered along lines walked edge-to-edge or corner-to-corner of a field.

The number of styles was counted for every flower collected. Each collection was tabulated, and cumulative records were kept, separately, for each plot from which repeated collections were taken. All ovaries with an atypical number of styles were preserved in formol–acetic-acid–alcohol as evidence of collection and for histological study.

Ovaries of most (66.9 percent) of the 21,669 flowers examined bore the typical five styles; style numbers for the remainder (33.1 percent) ranged as follows: 0, 1, 2, 3, 4, 6, 7, 8, 9, and 10 styles per ovary (Table 1). The number of carpels, placentae, and placental vascular strands of a given ovary, determined from paraffin sections, varied directly with the number of styles it bore, except for styleless ovaries and those with certain other irregularities.

Of 18 styleless ovaries sectioned, carpels ranging in number from three to seven, inclusive, were found. Similarly, the number of styles of a given ovary did not correspond always to the actual number of carpels. For example, ovaries with one to four styles, inclusive, could be expected to have, correspondingly, one to four carpels. However, any one of these might actually have five to eight (possibly more) carpels; this suggested that one or more styles of a particular ovary had failed to develop.

The typical, young, five-styled ovary of *Lychnis alba* has axile placentation with five carpellary septa connecting the ovary wall to the columnar placental region. Subsequently these septa break, and the whole central region (actually containing five placentae) thus detached from the ovary wall becomes the free-central placenta.

Except for stated irregularities, one-styled ovaries have one carpel, one locule, and one marginal placenta. Two-styled ovaries have two carpels and two locules, the placenta becoming free-central when the two oppositely placed carpellary septa break. Ovaries with three to ten styles, inclusive, develop typically.

The placental column of a typical five-styled, five-carpellate ovary has five prominent, equally spaced, radially prolonged vascular strands (appearing starlike in placenta cross sections) extending platelike throughout its length. These vascular strands vary directly with the number of carpels and placentae but not always with the number of styles of a given ovary.

Ovaries of *Lychnis alba* may have more carpels, placentae, and vascular strands than styles, but the reverse situation was not found.

Significant variations in style number appeared in every larger collection of *Lychnis alba* flowers examined during 1958; smaller collections sometimes produced fewer variations, most (and occasionally all) ovaries bearing five styles. Twenty-nine individual plants observed daily in a greenhouse throughout their entire flowering period from October 1958 through January 1959 exhibited a similar variance (*8*). Twenty-five of these produced ovaries bearing significant variations in style number (four to nine, inclusive); one was an androhermaphrodite; in one most ovaries bore five styles; and in two all ovaries bore five styles, strictly.

In this respect, one plot of *Lychnis alba* (West Liberty plot No. 5) proved especially interesting because the most complete range of variation in style numbers found in any one plot studied during 1958 (zero to ten, inclusive) occurred in the 4142 flowers collected from it. Two hundred and forty-one gynohermaphrodite flowers with styles ranging in number from three to eight, inclusive, were likewise found in this plot.

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Table 1. Data indicating the total number of *Lychnis alba* flowers collected from each general area, the spread of variations in style number, the number of examples and totals for each category of variation, and the grand total of all flowers examined during 1958.

No. of styles	No. of flowers: Iowa greenhouse, 19 May–23 June (*7*)	Iowa outdoors, 20 June–23 July	Minnesota outdoors, 1–27 Aug.	Total No. of flowers of given style No. from the three areas
0	0	8	24	32
1	0	13	14	27
2	0	13	31	44
3	4	46	88	138
4	149	218	391	758
5	2,607	4,967	6,933	14,507
6	317	1,766	2,454	4,537
7	64	661	712	1,437
8	5	90	68	163
9	1	13	10	24
10	0	2	0	2
Totals	3,147	7,797	10,725	21,669

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7. The plants were grown from seeds collected by Theodore VanBruggen near Indianola, Iowa, 21 June 1957.
8. The plants were grown from seeds collected from West Liberty plot No. 5 near West Liberty, Iowa, 23 July 1958.

9 February 1959

Incidence of Sex Chromatin in Gallus domesticus

Abstract. The presence of so-called sex chromatin has been demonstrated in the interphase nuclei of the cells of the domestic chicken (*Gallus domesticus*). Definite sex dimorphism was observed for the incidence of this nuclear component; the frequency of its occurrence in females was at least ten times that of its occurrence in the males, ranging from 22 percent in the duodenal muscle cells to 52 percent in the epidermal cells of a growing feather.

Considerable corroborative evidence for the existence of sex chromatin in mammals has been accumulating since Barr and Bertram (*1*) first drew attention to the "nuclear satellite" and its possible usefulness in establishing the genetic sex of an individual. The term *nuclear satellite* was subsequently (*2*) changed to *sex chromatin*. All the reports to date, of which those of Cantwell *et al.* (*3*) and of Osuchowska and Suminski (*4*) are among the latest, clearly indicate the sex-dimorphic nature of the distribution of sex chromatin. In mammals, it is the cells of genetic females that are richly provided with this strongly basophilic, Feulgen-positive material. In males, sex chromatin is either nonexistent or occurs only infrequently. One is not surprised, therefore, to find a generalization, suggested by Prince *et al.* (*5*), that sex chromatin is the heterochromatic portion of the 2 X chromosomes. More recently Klinger (*6*) came to the same conclusion. It should be recalled in this connection

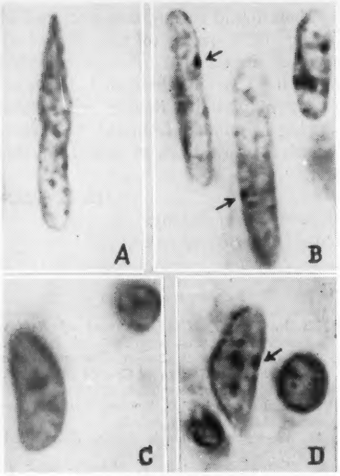

Fig. 1. Representative nuclei from the epidermis of a growing feather and muscle layer of the duodenum. *A* and *C,* from males; *B* and *D,* from females. Arrows point to sex chromatin.

that Smith, as early as 1945, presented evidence (*7*) showing that female sex in *Archips fumiferana,* a lepidopteran, could be identified on the basis of heteropycnosis in the intestine. He concluded that these heteropycnotic bodies are sex chromosomes—a somewhat puzzling deduction in view of the fact that in lepidoptera females are heterogametic. Thus, one would expect a still greater degree of heteropycnosis in the lepidopteran males (that is, if his postulate was correct), a situation contrary to the one observed by Smith.

The presently reported study (*8*) was undertaken to (i) examine the phenomenon of sex chromatin in relation to class Aves, in which the female sex is heterogametic (a situation just the reverse of that in mammals), and (ii), in case the results were positive, to use sex chromatin as a tool in studying the genetic sex of rather frequently occurring sex intergrades in the domestic poultry. On the basis of the interpretation of the published mammalian data, the expectation was that, if sex chromatin occurs in birds, it would be found to be characteristic, in the main, of quiescent nuclei in the male sex.

The study involved 3-week-old New Hampshire chickens. Specimens for histologic examination were obtained from the following organs and tissues: brain, spinal cord, liver, intestine, pancreas, gonads, skin, and feathers. The specimens were fixed in a mixture of formol–acetic-acid–alcohol (40 percent formaldehyde, glacial acetic acid, 95-percent EtOH, and distilled water in the ratio of 2:1:3:3, respectively), and stained with Harris' hematoxylin.

Of the tissues studied, smooth muscles in the duodenum and dermal and epidermal components at the base of a growing feather were found to be best for demonstrating the presence of sex chromatin in the chicken (Fig. 1). While there were individual differences among the birds in the incidence of sex chromatin, clear-cut dimorphism was unmistakable: in females, the sex chromatin was much more prevalent than in males (Table 1).

The duodenal and feather preparations also were subjected to Feulgen reagent as well as to ribonuclease digestion, followed by the Unna pyronin–methyl-green staining procedure. Both of these histochemical tests indicated the presence of deoxyribonucleic acid in the sex chromatin, a point which had been demonstrated earlier for the mammalian material (*9*). This fact, together with the general morphology of sex chromatin in the chicken (its extreme basophily and its occurrence only in the interphase nucleus where it is closely apposed to the nuclear membrane) led us to conclude that it is analogous to the sex chromatin of mammals.

If this point of view is accepted, then it makes untenable the suggestion (*1, 5, 10*) that sex chromatin is the heterochromatin of the two sex chromosomes; the somatic nuclei of the female chicken carry only a single sex chromosome.

On the basis of the observations reported above, we agree with the view of Witschi (*11*) that sex chromatin is not necessarily related to X chromosomes, although it is, clearly, an incompletely-sex-limited trait characterizing the female sex. Obviously, this generalization at present can only be applied to the mammalian and avian species thus far studied. The elaboration and possible modification of the concept, together with elucidation of the basic nature of sex chromatin, will have to await further studies.

Table 1. Frequencies (percentages) of occurrence of cells with identifiable sex chromatin.

Bird specimen No.	Feathers: Dermal	Feathers: Epidermal	Duodenal muscles
	Female		
1	44	51	28
2	40	46	21
3	39	55	15
4	31	52	22
5	36	56	22
Av.	35	52	22
Total No. of cells	1100	931	732
	Male		
1	1.6	3.5	4.7
2	4.8	5.4	3.8
3	1.1	2.1	2.9
4	0.4	5.2	1.2
5	1.2	1.0	0.6
Av.	1.9	3.4	2.6
Total No. of cells	938	946	782

I. L. Kosin
Hironori Ishizaki

Department of Poultry Science, State College of Washington, Pullman

References and Notes

1. M. L. Barr and E. G. Bertram, *Nature* 163, 677 (1949).
2. M. A. Graham and M. L. Barr, *Anat. Record* 112, 709 (1952).
3. G. E. Cantwell, E. F. Johnston, J. H. Zeller, *J. Heredity* 49, 199 (1958).
4. Z. Osuchowska and E. Suminski, *Folia Morphol.* 8, 195 (1957).
5. R. H. Prince, M. A. Graham, M. L. Barr, *Anat. Record* 122, 153 (1955).
6. H. P. Klinger, *Exptl. Cell Research* 14, 207 (1958).
7. S. G. Smith, *Sci. Agr.* 25, 566 (1945).
8. This report is Washington Agricultural Experiment Stations scientific paper, No. 1816, project No. 717. This study was supported in part by federal funds for regional research (W-7), under the amended Hatch Act. A portion of this material was presented at the 28th annual meeting of the Western Society of Naturalists, held 29–30 Dec. 1958, in Seattle, Washington.
9. M. L. Barr, L. F. Bertram, H. A. Lindsay, *Anat. Record* 107, 283 (1950).
10. L. Sachs and M. Danon, *Genetics* 28, 201 (1956).
11. E. Witschi, *Proc. Intern. Genet. Symposium, Tokyo and Kyoto, Japan* 133 (1956).

16 February 1959

Letters

(Continued from page 4)

Whether, as Reynolds and Meyers claim, we have erred in our interpretation of the meaning and implications of their work (*1, 2*) can best be judged by reference to what we said, and to their published reports, on which our remarks were based. We wrote (*3*):

"Believing that fungal infection always occurs prior to attack by marine wood borers, especially *Limnoria,* they [Meyers and Reynolds] *suggested* that there *might* be a relationship between fungi and wood-destroying animals." (Italics added).

Both parts of this sentence require comment in the light of Reynolds and Meyers' objections. First, the only *belief* that we credit to these authors is that of holding that fungal infection of submerged wood always precedes marine borer attack. Our statement that this is their belief is based upon the following three quotations. In the concluding paragraph of their article in *Science* (*1*) they said:

"The vigorous fungal infestation of submerged wood prior to borer attack represents a biological phenomenon that investigators of marine wood destruction should not ignore. In northern areas, winter fungal infestation of wood is evident. Hence, in the early spring, when borer activity increases rapidly, the animals have available a wood substrate thoroughly infected by a variety of marine fungi. The interrelationships within this biota are being studied in our laboratory."

And in the same article they wrote:

"Vigorous attack [by fungi] upon submerged wood in boreal and northern temperate areas during winter months is accompanied by no, or very slight, borer damage. A similar situation occurs in subtropical localities, however, with a considerably shorter period of fungal attack prior to borer infestation."

Finally, the following sentences appear in another article (*2*, p. 10, paragraph one):

"The fungal infection that occurs before the borers attack the wood has interesting biological implications. In northern areas, especially, it may facilitate the activities of the borers, not only by making it easier for them to enter the wood, but also by providing them with a source of food."

We still think that it is fair to say that Reynolds and Meyers indicated a belief that fungal infection always precedes attack by marine borers. Concerning the second half of our sentence, we believe that the excerpts quoted above and other comments in the two articles cited do support our statement that Reynolds and Meyers suggest that there may be

a relationship between marine fungi and marine wood borers.

With reference to the three specific objections enumerated in their letter, we will respond to the second one first, for here Reynolds and Meyers have legitimate grounds for complaint. In our article in *Science*, we inadvertently cited the report that "*Limnoria* is unable to attack sterilized wood" as reference number 3 [Reynolds and Meyers (*2*)], but it should have been cited as reference 4 [Schafer and Lane (*4*)]. We apologize for this typographical error in the bibliographic citation. To set the record straight, Schafer and Lane (*4*), reporting work done at the Marine Laboratory of the University of Miami, state in their abstract: "*Limnoria* of both sexes and all ages did not survive when they were allowed to feed only on sterile wood in sterile sea water. No fecal pellets were produced under the conditions of this experiment." Supporting evidence is given in the text of the paper.

Reynolds and Meyers' first listed objection is that we included their work among the cases where we said it has been ". . . stated, suggested, or implied that marine wood-boring animals do not attack wood or become established in it unless the wood is first invaded and 'conditioned' by marine fungi" (*3*). Immediately preceding this comment we cited work from three different groups of investigators. Perhaps it would have been more precise to say that Becker, Kampf and Kohlmeyer (*5*) stated, Schafer and Lane (*4*) suggested, and Reynolds and Meyers (*1, 2*) implied.

It is our opinion that Reynolds and Meyers' work reported in their two papers does indeed convey the implication that marine wood-boring animals do not attack wood or become established in it unless the wood is first invaded and "conditioned" by marine fungi. A careful rereading of these papers has not altered this opinion. Independent evidence that we are not alone in this interpretation may be found in the table of contents of the issue of *ONR Research Reviews* in which one of their papers (*2*) appears. Following the title is this explanatory statement (authorship unknown):

"Investigations now underway show that marine fungi are one of the chief contributors to the deterioration of submerged wood. They not only vigorously degrade wood, but also prepare it for the entrance of other wood destroyers."

Finally, regarding the third point made by Reynolds and Meyers in their letter, we did not claim that they "expressed a belief" that *Limnoria* will not attack wood until its surface has been "conditioned." (We do not believe this either!) Our reference to their work in this connection was only to the observation that a period of time elapses between the exposure of wood to sea water and its invasion by *Limnoria*.

The many questions of keen interest that arise from the results we have submitted, conflicting as they do with those from other investigators, deserve fuller discussion than is appropriate in this letter or was possible in our report. Until such further discussion can be engaged in, we wish only to make our position abundantly clear. We have undertaken a critical evaluation of just one point: whether there is any relationship between marine fungi and *Limnoria* attack. Our results indicate that there is not. We do not believe that this closes the case; it is necessary now to determine why our results differ from those of other workers.

D. L. Ray
D. E. Stuntz
Departments of Zoology and *Botany, University of Washington, Seattle*

References

1. S. P. Meyers and E. S. Reynolds, *Science* 126, 969 (1957).
2. E. S. Reynolds and S. P. Meyers, *Office Naval Research, Research Revs.* (Dec. 1957), pp. 6–11.
3. D. L. Ray and D. E. Stuntz, *Science* 129, 93 (1959).
4. R. D. Schafer and C. E. Lane, *Bull. Marine Sci. Gulf and Caribbean* 7, 289 (1957).
5. G. Becker, W.-D. Kampf, J. Kohlmeyer, *Naturwissenschaften* 17, 473 (1957).

Meetings

Forthcoming Events

August

1–8. World Congress of Esperantists, 44th, Warsaw, Poland. (Office of Intern. Conferences, Dept. of State, Washington 25.)

4–5. American Astronautical Soc., 2nd annual western, Los Angeles, Calif. (A. P. Mayernik, AAS, 6708 53 Rd., Maspeth 78, N.Y.)

6–8. Human Pituitary Hormones, colloquium (by invitation only), Buenos Aires, Argentina. (G. E. W. Wolstenholme, Ciba Foundation, 41 Portland Place, London W.2, England.)

9–12. American Soc. of Mechanical Engineers (Heat Transfer Div.), conf., Storrs, Conn. (D. B. MacDougall, ASME, 29 West 39 St., New York 18.)

9–15. Physiological Sciences, 21st intern. cong., Buenos Aires, Argentina. (C. F. Schmidt, Univ. of Pennsylvania School of Medicine, Philadelphia 4.)

10–13. National Medical Assoc., Detroit, Mich. (J. T. Givens, 1108 Church St., Norfolk, Va.)

10–13. Society of Automotive Engineers, natl. West Coast meeting, Vancouver, B.C., Canada. (R. W. Crory, Meetings Operation Dept., SAE, 485 Lexington Ave., New York 17.)

16–19. Botanical Nomenclature, discussions (Intern. Bureau for Plant Taxonomy and Nomenclature), Montreal, Canada. (J. Rousseau, Natl. Museum, Ottawa, Canada.)

16–21. American Pharmaceutical Assoc., Cincinnati, Ohio. (R. P. Fischelis, APA, 2215 Constitution Ave., NW, Washington 7.)

17. Ultrasonics, natl. symp., San Francisco, Calif. (L. G. Cumming, Inst. of Radio Engineers, 1 E. 79 St., New York 21.)

17–21. Pacific Southwest Assoc. of Chemistry Teachers, Pacific Grove, Calif. (W. A. Craig, 416 N. Citrus Ave., Los Angeles 36, Calif.)

17–22. Logopedics and Phoniatrics, 11th intern. cong., London, England. (Miss P. Carter, 46 Canonbury Square, London N.1, England.)

19–26. Refrigeration, 10th intern. cong., Copenhagen, Denmark. (M. Kondrup, Danish Natl. Committee, Intern. Congress of Refrigeration, P.O. Box 57, Roskilde, Denmark.)

19–29. Botanical Cong., 9th intern., Montreal, Canada. (C. Frankton, Secretary-General, 9th Intern. Botanical Cong., Science Service Bldg., Ottawa, Ontario, Canada.)

19–29. International Assoc. of Wood Anatomists, Montreal, Canada. (IAWA, Laboratorium für Holzforschung E.T.H. Universitatstrasse 2, Zurich, Switzerland.)

19–29. Mycological Soc. of America, Montreal, Canada. (E. S. Beneke, Dept. of Botany and Plant Pathology, Michigan State Univ., E. Lansing.)

19–29. Phycological Soc. of America, Montreal, Canada. (W. A. Daily, Dept. of Botany, Butler Univ., Indianapolis 7, Ind.)

20–22. Rocky Mountain Radiological Soc., Denver, Colo. (J. H. Freed, 4200 E. Ninth Ave., Denver 20.)

20–25. Chemical Thermodynamics, symp., Wattens, Austria. (F. Vorländer, Deutsche Bunsen-Gesellschaft, Carl-Bosh-Haus, Varrentrappstrasse, 40–42, Frankfort a.M., Germany.)

20–27. Therapeutics, symp., Gardone, Italy. (R. Morf, c/o Sandoz S.A., Basel 13, Switzerland.)

20–2. Limnological Cong., 14th intern., Vienna and Salzburg, Austria. (Secretary, 14th Intern. Limnological Congress, Biologische Station, Lunz am See, Austria.)

23–26. American Farm Economic Assoc., Ithaca, N.Y. (C. D. Kearl, Dept. of Agricultural Economics, Warren Hall, Cornell Univ., Ithaca.)

23–27. Veterinary Medicine, 3rd Pan-American Cong., Kansas City, Mo. (B. D. Blood, Pan-American Congresses of Veterinary Medicine, P.O. Box 99, Azuk, Buenos Aires Province, Argentina.)

24–26. American Accounting Assoc., Boulder, Colo. (C. Cox, 437 Hagerty Hall, Ohio State Univ., Columbus 10.)

24–26. Anti-Submarine Warfare (classified), symp., San Diego, Calif. (R. R. Dexter, Inst. of the Aeronautical Sciences, 2 E. 64 St., New York 21.)

24–26. Dynamics of Conducting Fluids, (American Rocket Soc., and Northwestern Univ.), Evanston, Ill. (J. J. Harford, ARS, 500 Fifth Ave., New York 36.)

24–27. American Hospital Assoc., New York, N.Y. (E. L. Crosby, 18 E. Division St., Chicago, Ill.)

24–28. Australian and New Zealand Assoc. for the Advancement of Science, 34th cong., Perth, Western Australia. (J. R. A. McMillan, Science House, 157 Gloucester St., Sydney, Australia.)

24–29. Infrared Spectroscopy Inst., 10th annual, Nashville, Tenn. (N. Fuson, Director, Infrared Spectroscopy, Fisk Univ., Nashville 8.)

24–29. International Assoc. for Hydraulic Research, cong., Montreal, Canada. (IAHR, c/o Laboratoire Hydraulique, Raam 61, Delft, Netherlands.)

24–29. Ionization Phenomena in Gases, 4th intern. conf., Upsala, Sweden. (A. Nilsson, Secretary-General, Inst. of Physics, Upsala, Sweden.)

24–29. Polarography, 2nd intern. cong., Cambridge, England. (Mrs. B. Lamb, Chemistry Lab., Evershed & Vignoles, Corner of Iveagh Ave., N. Circular Rd., London N.W.10, England.)

24–30. Modern Systems for Detecting and Evaluating Optical Radiation (Intern. Optical Commission), symp., Stockholm, Sweden. (S. S. Ballard, Dept. of Physics, Univ. of Florida, Gainesville.)

25–27. Petroleum Industry Conf., AIEE, Long Beach, Calif. (N. S. Hibshman, AIEE, 33 W. 39 St., New York 18.)

25–28. Alaskan Science Conf., Alaskan Div., AAAS, 10th, Juneau. (N. J. Wilimovsky, Bur. of Commercial Fisheries, Box 2021, Juneau.)

25–28. American Dietetic Assoc., 42nd annual, Los Angeles, Calif. (Miss R. M. Yakel, ADA, 620 N. Michigan Ave., Chicago 11, Ill.)

25–30. American Ornithologists' Union, Regina, Saskatchewan, Canada. (H. G. Deignan, Div. of Birds, U.S. National Museum, Washington 25.)

26–29. International Assoc. of Milk and Food Sanitarians, Glenwood Springs, Colo. (V. T. Foley, Health Dept., Kansas City, Mo.)

26–29. International Union of Pure and Applied Chemistry, 20th conf., Munich, Germany. (Div. of Chemistry and Chemical Technology, Natl. Research Council, Washington 25.)

27–29. American Assoc. of Clinical Chemists, 11th annual, Cleveland, Ohio. (A. Hainline, Jr., AACC, Cleveland Clinic Foundation, 2020 E. 93 St., Cleveland 6.)

27–29. American Physical Soc., Hawaii. (K. K. Darrow, APS, Columbia Univ., New York 27.)

28–29. Weather Modification (with American Soc. of Civil Engineers), conf., Denver, Colo. (H. G. Houghton, AMS, Dept. of Meteorology, Massachusetts Inst. of Technology, Cambridge 39, Mass.)

28–30. American Folklore Soc., annual, Albany and Cooperstown, N.Y. (MacE. Leach, 110 Bennett Hall, Univ. of Pennsylvania, Philadelphia 4.)

28–31. Astronomical League, Denver, Colo. (R. Dakin, 720 Victor Rd., Pittsford, N.Y.)

28–4. International Union for Scientific Study of Population, cong., Vienna, Austria. (F. Lorimer, Dept. of Sociology, American Univ., Washington, D.C.)

30–3. American Inst. of Biological Sciences, annual, University Park, Pa. (H. T. Cox, AIBS, 2000 P St., NW, Washington 6.)

30–4. American Cong. of Physical Medicine and Rehabilitation, Minneapolis, Minn. (Miss D. C. Augustin, 30 N. Michigan Ave., Chicago 2, Ill.)

30–4. Laurentian Hormone Conf., Mont Tremblant, Quebec, Canada. (G. Pincus, 222 Maple Ave., Shrewsbury, Mass.)

30–4. Medical Education, 2nd world conf., Chicago, Ill. (World Medical Assoc., 10 Columbus Circle, New York 19.)

30–5. World Federation for Mental Health, 12th annual, Barcelona, Spain. (Miss E. M. Thornton, Secretary-General, WFMH, 19, Manchester St., London W.1, England.)

30–6. History of Science, 9th intern. cong., Barcelona and Madrid, Spain. (J. Vernet, via Layetona 141, Barcelona.)

30–6. Residues on Crops and/or the Problem of Insect Resistance to Insecticides, symp., Munich, Germany. (R. Morf, Secretary-General, IUPAC, c/o Sandoz S. A., Basel, Switzerland.)

31–3. Biological Photographic Assoc., Montreal, Canada. (Miss J. H. Waters, P.O. Box 1668, Grand Central Station, New York 17.)

31–3. Mathematical Assoc. of America, 40th summer meeting, Salt Lake City, Utah. (H. M. Gehman, MAA, Univ. of Buffalo, Buffalo 14, N.Y.)

31–4. Haematin Enzymes, symp. (by invitation), Canberra, Australia. (A. H. Ennar, John Curtin School of Medical Research, Australian National Univ., Canberra.)

(See issue of 19 June for comprehensive list)

New Products

The information reported here is obtained from manufacturers and from other sources considered to be reliable, and it reflects the claims of the manufacturer or other source. Neither Science *nor the writer assumes responsibility for the accuracy of the information. A coupon for use in making inquiries concerning the items listed appears on page 54.*

■ RECORDING SYSTEM for strain gages plots strain versus load for 24 to 96 strain gage channels on a continuous paper loop. Digital read-out can also be provided. The paper loop can be supplied in length to match the number of channels being scanned. Individual gage-factor and range-selector controls are provided for each channel. Polarity is automatically indicated, and the full width of the paper is utilized to plot tension or compression. The contact resistance of the switches does not influence accuracy. B & F Instruments, Inc., Dept. 894)

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■ PLIABILITY TESTER simulates the action of wrapping a paper-like material around an object and measures the material's resistance to this operation. The instrument is portable and self-contained, and it includes a sample cutter. The device operates by measuring the force on a piston required to drive a 10-in.-diameter sample through a ring. Force is read on a calibrated dial gage. (American Instrument Co., Inc., Dept. 899)

■ LIGHT BOX for illumination of transparent or translucent drawings and charts is designed to fit into a desk drawer. Illuminated area is sufficient for 8½ by 11-in. sheets. Fluorescent tubes are used for cool operation, and provision is made for tilting to a convenient angle. (Instruments for Research and Industry, Dept. 900)

■ SEDIMENT-DENSITY PROBE operates on the principle that the scattering and absorption of gamma rays is a function of the density of the medium. Range of the instrument is 20 to 130 lb/ft³. The device consists of a source, counter, and a lead shield to isolate the counter from the unscattered beam. The instrument is immersion-proof and includes a built-in preamplifier to permit remote recording. Measurements accurate to better than 1 lb/ft³ are said to be possible with measuring time of 1 min. (Technical Operations Inc., Dept. 901)

■ PRESSURE TELEMETER for studying intraluminal pressures is an ingestible, reusable capsule 20 mm long and 8 mm in diameter. The device consists of a battery-powered, transistorized oscillator, that is frequency-modulated by pressures acting on a diaphragm. An external receiver demodulates the signal for display on an oscilloscope or for recording. Pressures up to 200 cm-H_2O are said to be detected with accuracy of ±3 percent of full scale. Battery life is 72 hr. (Airborne Instruments Laboratory, Dept. 905)

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For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

PROFESSIONAL SERVICES

3 July 1959

Readers' Service

Information Requisition

Use this easy self-mailer to obtain further information about items or literature from the New Products section as well as from advertised products.

NEW PRODUCTS

Circle below desired number corresponding to:

894	889	881	911	896	898	899	900
901	905	908	909	910	915	916	923

ADVERTISERS IN THIS ISSUE

In the below list, check page number of advertiser from whom you would like more information. If more than one item appears in ad, letters **A**, **B**, **C** are used to indicate particular items available in order of appearance in advertisement. Where more than one ad appears on page, **U** indicates upper ad, **L** lower ad, **I** inside ad, **M** middle ad, and **O** outside ad. The covers are designated by **IFC** (inside front cover), **IBC** (inside back cover), and **OBC** (outside back cover). Advertisements in Personnel Placement and Market Place are not keyed. A multiplicity of items is indicated by *. Readers are requested to specify on this coupon the particular item in which they are interested; otherwise, the request cannot be processed.

☐ IFC	☐ 3,A	☐ 3,B	☐ 3,C	☐ 4
☐ 5,A	☐ 5,B	☐ 5,C	☐ 6	☐ 8*
☐ 45,U-A	☐ 45,U-B	☐ 45,L	☐ 46,U	☐ 47
☐ 49,UI	☐ 49,UO	☐ 51,UO	☐ 51,L	☐ 52
☐ IBC,UI	☐ IBC,UO*	☐ IBC,L	☐ OBC	

PROFESSIONAL SERVICES

BOOKS AND MAGAZINES

SUPPLIES AND EQUIPMENT

GME

SQUARE FRACTIONATOR

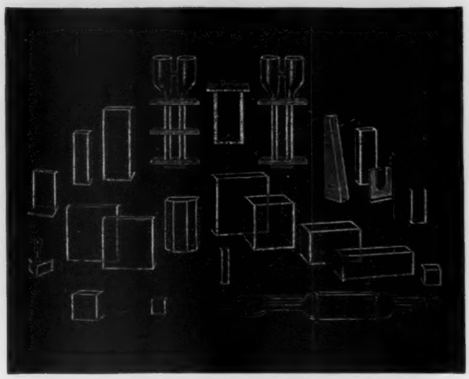
collects directly into test tube racks

- ★ Accurate collection in 225 test tubes
- ★ 450 tedious test tube transfers are eliminated
- ★ Equipped with 3 racks — each with 5 rows, 15 tubes per row
- ★ Improved volumetric unit
- ★ Timer or N.I.L. drop counter attachment available

The racks themselves, with all the test tubes in the order collected, may be removed from the fractionator for further processing.

GILSON MEDICAL ELECTRONICS
On Madison's West Beltline Highway
Middleton, Wisconsin

GLASS ABSORPTION CELLS made by KLETT



SCIENTIFIC APPARATUS
Klett-Summerson Photoelectric Colorimeters—Colorimeters — Nephelometers — Fluorimeters—Bio-Colorimeters — Comparators — Glass Standards—Klett Reagents.

Klett Manufacturing Co.
179 East 87 Street, New York, New York

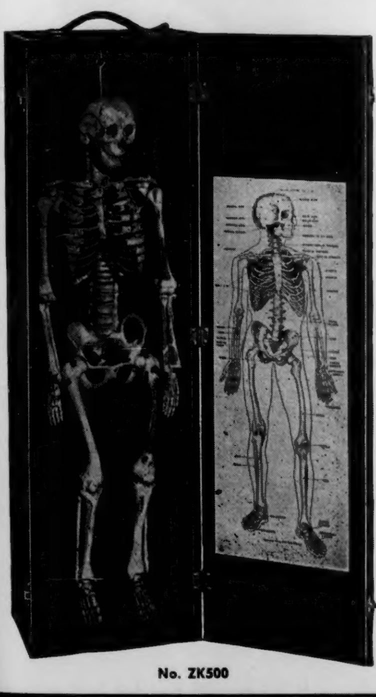
SYNTHETIC MINIATURE HUMAN SKELETON

ANATOMICALLY ACCURATE

Only 26 Inches Tall

Weighs Less Than 20 Pounds

Accurately Scaled In Durable, Washable Synthetic Bone



No. ZK500

Designed for use in high school biology courses, the miniature skeleton has proved of value in psychology, health, safety, first aid, and physical education courses. The low price enables the smaller schools to have at least one skeleton in the science department. The skeleton, with wooden case, weighs less than 20 pounds making it easy to carry from room to room.

The wooden case is constructed to permit the rotation of the skeleton within the case. An illustrated key card on the door identifies the principal bones. This arrangement permits a student to study the guide and skeleton together in order to more easily understand the skeleton. If desired, the skeleton can be removed from the case and hung in a more convenient place. The hook on the skull provides for attachment to other types of support.

Each skeleton includes an attractive wooden case, plastic skeleton cover, and an illustrated key card.

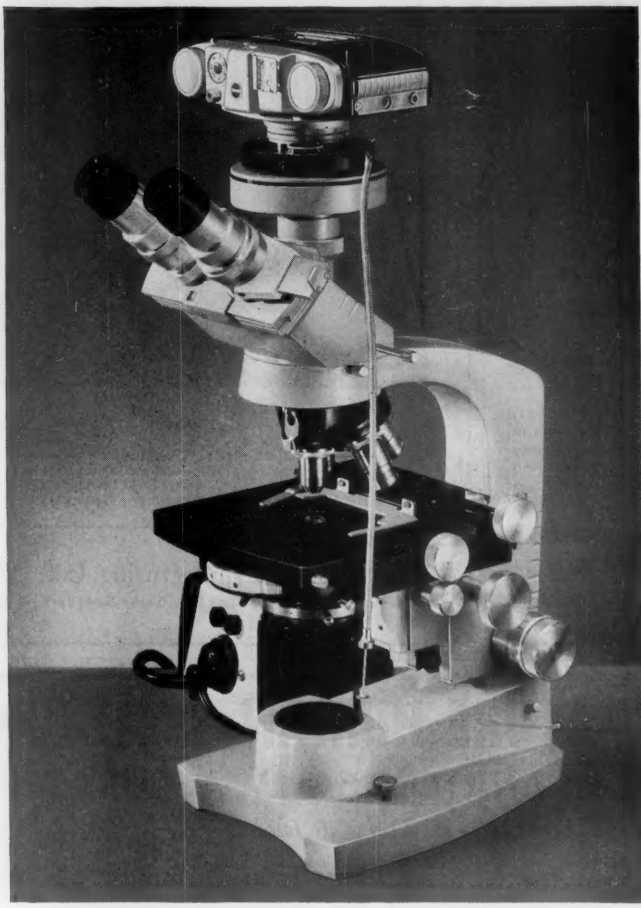
ZK500. MINIATURE SKELETON, Painted. The muscular origins are painted in red, and the muscular insertions are in blue on one side of the skeleton. Complete, with wooden case, plastic skeleton cover, and 2 illustrated key cards. Each, $137.00

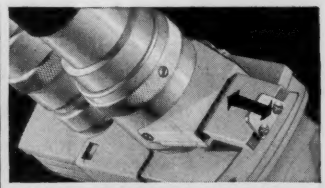
ZK510. MINIATURE SKELETON. The skeleton is the same as ZK500, but the muscular origins and insertions are not painted. Many teachers prefer to paint the muscular insertions and origins themselves, and the surfaces of these skeletons readily accept paint. Complete with attractive wooden case, illustrated key card, and plastic cover. Each, $115.00

Full, Life-Size Skeleton available at $212.00.

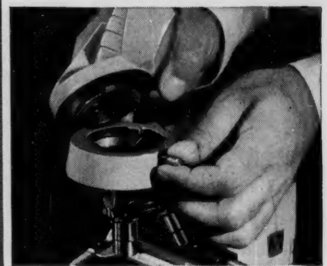
W. M. WELCH SCIENTIFIC COMPANY
DIVISION OF W. M. WELCH MANUFACTURING COMPANY
ESTABLISHED 1880
1515 Sedgwick Street, Dept. E, Chicago 10, Illinois, U.S.A.
Manufacturers of Scientific Instruments and Laboratory Apparatus

Here's why AO Phasestar offers you more!





New Bertrand Lens Built-in Bertrand lens is now supplied as standard on all binocular and trinocular Phasestars to provide new convenience. You slide lens into position in eyepiece tube and raise or lower to focus quickly on diffraction plate at back aperture of objective.



Interchangeable, Rotatable Bodies Your choice of interchangeable, rotatable, monocular, binocular or trinocular bodies. Simply loosen thumb screw to rotate (full 360°) or interchange. Special inclined monocular body with vertical photographic tube also available.

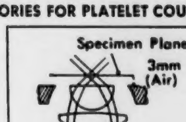
Interchangeable Stages You loosen single set screw to remove and interchange stages . . . your choice of graduated or ungraduated mechanical or MICRO-GLIDE stages.

The AO Spencer Phasestar is the most versatile phase microscope ever developed. Beginning with a basic Phasestar stand, you can select from a wide choice of interchangeable bodies, stages, optics and phase accessories to make up the specific model that meets your exact needs...all in all, more than 50 possible combinations or models to choose from. And whatever the model you choose, you're assured of superior AO Spencer quality *plus* matchless convenience, comfort and versatility.

Often particular phase applications require specific equipment and phase contrast objectives. Before you select your phase microscope and accessories consult your AO Sales Representative. He's qualified to help you select the microscope and equipment you need to do the job. There's no obligation, of course.

AO SPENCER PHASE ACCESSORIES FOR PLATELET COUNTS

The use of phase contrast for blood platelet counts is increasing in acceptance and application. The longer working distance required with the phase hemacytometer can be obtained with special AO Spencer long working distance accessories that provide up to 7mm working distance in air or 10½mm in glass.



SPENCER

American Optical Company

INSTRUMENT DIVISION, BUFFALO 15, NEW YORK

Dept. S-1

☐ I would like to review a specific phase microscopy problem. Please have AO Sales Representative call.

☐ Please send copy of Phasestar Brochure.

Name____________________

Address____________________

City__________ Zone____ State________